

Antisense RNAs and DNAs can be used as therapeutic agents for blocking the expression of certain genes *in vivo*. It has already been shown that short antisense oligonucleotides can be imported into cells where they act as inhibitors, despite their low intracellular concentrations caused by their restricted uptake by the cell membrane. (Zamecnik *et al.*, Proc. Natl. Acad. Sci. USA 83:4143-4146 [1986]). The oligonucleotides can be modified to enhance their uptake, e.g. by substituting their negatively charged phosphodiester groups by uncharged groups.

There are a variety of techniques available for introducing nucleic acids into viable cells. The techniques vary depending upon whether the nucleic acid is transferred into cultured cells *in vitro*, or *in vivo* in the cells of the intended host. Techniques suitable for the transfer of nucleic acid into mammalian cells *in vitro* include the use of liposomes, electroporation, microinjection, cell fusion, DEAE-dextran, the calcium phosphate precipitation method, etc. The currently preferred *in vivo* gene transfer techniques include transfection with viral (typically retroviral) vectors and viral coat protein-liposome mediated transfection (Dzau *et al.*, Trends in Biotechnology 11, 205-210 [1993]). In some situations it is desirable to provide the nucleic acid source with an agent that targets the target cells, such as an antibody specific for a cell surface membrane protein or the target cell, a ligand for a receptor on the target cell, etc. Where liposomes are employed, proteins which bind to a cell surface membrane protein associated with endocytosis may be used for targeting and/or to facilitate uptake, e.g. capsid proteins or fragments thereof tropic for a particular cell type, antibodies for proteins which undergo internalization in cycling, proteins that target intracellular localization and enhance intracellular half-life. The technique of receptor-mediated endocytosis is described, for example, by Wu *et al.*, J. Biol. Chem. 262, 4429-4432 (1987); and Wagner *et al.*, Proc. Natl. Acad. Sci. USA 87, 3410-3414 (1990). For review of gene marking and gene therapy protocols see Anderson *et al.*, Science 256, 808-813 (1992).

The PRO polypeptides described herein may also be employed as molecular weight markers for protein electrophoresis purposes.

The nucleic acid molecules encoding the PRO polypeptides or fragments thereof described herein are useful for chromosome identification. In this regard, there exists an ongoing need to identify new chromosome markers, since relatively few chromosome marking reagents, based upon actual sequence data are presently available. Each PRO nucleic acid molecule of the present invention can be used as a chromosome marker.

The PRO polypeptides and nucleic acid molecules of the present invention may also be used for tissue typing, wherein the PRO polypeptides of the present invention may be differentially expressed in one tissue as compared to another. PRO nucleic acid molecules will find use for generating probes for PCR, Northern analysis, Southern analysis and Western analysis.

The PRO polypeptides described herein may also be employed as therapeutic agents. The PRO polypeptides of the present invention can be formulated according to known methods to prepare pharmaceutically useful compositions, whereby the PRO product hereof is combined in admixture with a pharmaceutically acceptable carrier vehicle. Therapeutic formulations are prepared for storage by mixing the active ingredient having the desired degree of purity with optional physiologically acceptable carriers, excipients or stabilizers (Remington's Pharmaceutical Sciences 16th edition, Osol, A. Ed. (1980)), in the form of lyophilized formulations or aqueous solutions. Acceptable carriers, excipients or stabilizers are nontoxic to recipients at the

dosages and concentrations employed, and include buffers such as phosphate, citrate and other organic acids; antioxidants including ascorbic acid; low molecular weight (less than about 10 residues) polypeptides; proteins, such as serum albumin, gelatin or immunoglobulins; hydrophilic polymers such as polyvinylpyrrolidone, amino acids such as glycine, glutamine, asparagine, arginine or lysine; monosaccharides, disaccharides and other carbohydrates including glucose, mannose, or dextrans; chelating agents such as EDTA; sugar alcohols such as mannitol or sorbitol; salt-forming counterions such as sodium; and/or nonionic surfactants such as TWEEN<sup>TM</sup>, PLURONICS<sup>TM</sup> or PEG.

The formulations to be used for *in vivo* administration must be sterile. This is readily accomplished by filtration through sterile filtration membranes, prior to or following lyophilization and reconstitution.

Therapeutic compositions herein generally are placed into a container having a sterile access port, for example, an intravenous solution bag or vial having a stopper pierceable by a hypodermic injection needle.

The route of administration is in accord with known methods, e.g. injection or infusion by intravenous, intraperitoneal, intracerebral, intramuscular, intraocular, intraarterial or intralesional routes, topical administration, or by sustained release systems.

Dosages and desired drug concentrations of pharmaceutical compositions of the present invention may vary depending on the particular use envisioned. The determination of the appropriate dosage or route of administration is well within the skill of an ordinary physician. Animal experiments provide reliable guidance for the determination of effective doses for human therapy. Interspecies scaling of effective doses can be performed following the principles laid down by Mordenti, J. and Chappell, W. "The use of interspecies scaling in toxicokinetics" In *Toxicokinetics and New Drug Development*, Yacobi et al., Eds., Pergamon Press, New York 1989, pp. 42-96.

When *in vivo* administration of a PRO polypeptide or agonist or antagonist thereof is employed, normal dosage amounts may vary from about 10 ng/kg to up to 100 mg/kg of mammal body weight or more per day, preferably about 1 µg/kg/day to 10 mg/kg/day, depending upon the route of administration. Guidance as to particular dosages and methods of delivery is provided in the literature; see, for example, U.S. Pat. Nos. 4,657,760; 5,206,344; or 5,225,212. It is anticipated that different formulations will be effective for different treatment compounds and different disorders, that administration targeting one organ or tissue, for example, may necessitate delivery in a manner different from that to another organ or tissue.

Where sustained-release administration of a PRO polypeptide is desired in a formulation with release characteristics suitable for the treatment of any disease or disorder requiring administration of the PRO polypeptide, microencapsulation of the PRO polypeptide is contemplated. Microencapsulation of recombinant proteins for sustained release has been successfully performed with human growth hormone (rhGH), interferon-(rhIFN- ), interleukin-2, and MN rgp120. Johnson et al., *Nat. Med.*, 2:795-799 (1996); Yasuda, *Biomed. Ther.*, 27:1221-1223 (1993); Hora et al., *Bio/Technology*, 8:755-758 (1990); Cleland, "Design and Production of Single Immunization Vaccines Using Polylactide Polyglycolide Microsphere Systems," in *Vaccine Design: The Subunit and Adjuvant Approach*, Powell and Newman, eds, (Plenum Press: New York, 1995), pp. 439-462; WO 97/03692, WO 96/40072, WO 96/07399; and U.S. Pat. No. 5,654,010.

The sustained-release formulations of these proteins were developed using poly-lactic-coglycolic acid (PLGA) polymer due to its biocompatibility and wide range of biodegradable properties. The degradation products of PLGA, lactic and glycolic acids, can be cleared quickly within the human body. Moreover, the degradability of this polymer can be adjusted from months to years depending on its molecular weight and composition. Lewis, "Controlled release of bioactive agents from lactide/glycolide polymer," in: M. Chasin and R. Langer (Eds.), Biodegradable Polymers as Drug Delivery Systems (Marcel Dekker: New York, 1990), pp. 1-41.

This invention encompasses methods of screening compounds to identify those that mimic the PRO polypeptide (agonists) or prevent the effect of the PRO polypeptide (antagonists). Screening assays for antagonist drug candidates are designed to identify compounds that bind or complex with the PRO polypeptides encoded by the genes identified herein, or otherwise interfere with the interaction of the encoded polypeptides with other cellular proteins. Such screening assays will include assays amenable to high-throughput screening of chemical libraries, making them particularly suitable for identifying small molecule drug candidates.

The assays can be performed in a variety of formats, including protein-protein binding assays, biochemical screening assays, immunoassays, and cell-based assays, which are well characterized in the art.

All assays for antagonists are common in that they call for contacting the drug candidate with a PRO polypeptide encoded by a nucleic acid identified herein under conditions and for a time sufficient to allow these two components to interact.

In binding assays, the interaction is binding and the complex formed can be isolated or detected in the reaction mixture. In a particular embodiment, the PRO polypeptide encoded by the gene identified herein or the drug candidate is immobilized on a solid phase, e.g., on a microtiter plate, by covalent or non-covalent attachments. Non-covalent attachment generally is accomplished by coating the solid surface with a solution of the PRO polypeptide and drying. Alternatively, an immobilized antibody, e.g., a monoclonal antibody, specific for the PRO polypeptide to be immobilized can be used to anchor it to a solid surface. The assay is performed by adding the non-immobilized component, which may be labeled by a detectable label, to the immobilized component, e.g., the coated surface containing the anchored component. When the reaction is complete, the non-reacted components are removed, e.g., by washing, and complexes anchored on the solid surface are detected. When the originally non-immobilized component carries a detectable label, the detection of label immobilized on the surface indicates that complexing occurred. Where the originally non-immobilized component does not carry a label, complexing can be detected, for example, by using a labeled antibody specifically binding the immobilized complex.

If the candidate compound interacts with but does not bind to a particular PRO polypeptide encoded by a gene identified herein, its interaction with that polypeptide can be assayed by methods well known for detecting protein-protein interactions. Such assays include traditional approaches, such as, e.g., cross-linking, co-immunoprecipitation, and co-purification through gradients or chromatographic columns. In addition, protein-protein interactions can be monitored by using a yeast-based genetic system described by Fields and co-workers (Fields and Song, Nature (London), 340:245-246 (1989); Chien et al., Proc. Natl. Acad. Sci. USA, 88:9578-9582 (1991)) as disclosed by Chevray and Nathans, Proc. Natl. Acad. Sci. USA, 89: 5789-5793 (1991). Many

transcriptional activators, such as yeast GAL4, consist of two physically discrete modular domains, one acting as the DNA-binding domain, the other one functioning as the transcription-activation domain. The yeast expression system described in the foregoing publications (generally referred to as the "two-hybrid system") takes advantage of this property, and employs two hybrid proteins, one in which the target protein is fused to the DNA-binding domain of GAL4, and another, in which candidate activating proteins are fused to the activation domain. The expression of a GAL1-*lacZ* reporter gene under control of a GAL4-activated promoter depends on reconstitution of GAL4 activity via protein-protein interaction. Colonies containing interacting polypeptides are detected with a chromogenic substrate for  $\beta$ -galactosidase. A complete kit (MATCHMAKER™) for identifying protein-protein interactions between two specific proteins using the two-hybrid technique is commercially available from Clontech. This system can also be extended to map protein domains involved in specific protein interactions as well as to pinpoint amino acid residues that are crucial for these interactions.

Compounds that interfere with the interaction of a gene encoding a PRO polypeptide identified herein and other intra- or extracellular components can be tested as follows: usually a reaction mixture is prepared containing the product of the gene and the intra- or extracellular component under conditions and for a time allowing for the interaction and binding of the two products. To test the ability of a candidate compound to inhibit binding, the reaction is run in the absence and in the presence of the test compound. In addition, a placebo may be added to a third reaction mixture, to serve as positive control. The binding (complex formation) between the test compound and the intra- or extracellular component present in the mixture is monitored as described hereinabove. The formation of a complex in the control reaction(s) but not in the reaction mixture containing the test compound indicates that the test compound interferes with the interaction of the test compound and its reaction partner.

To assay for antagonists, the PRO polypeptide may be added to a cell along with the compound to be screened for a particular activity and the ability of the compound to inhibit the activity of interest in the presence of the PRO polypeptide indicates that the compound is an antagonist to the PRO polypeptide. Alternatively, antagonists may be detected by combining the PRO polypeptide and a potential antagonist with membrane-bound PRO polypeptide receptors or recombinant receptors under appropriate conditions for a competitive inhibition assay. The PRO polypeptide can be labeled, such as by radioactivity, such that the number of PRO polypeptide molecules bound to the receptor can be used to determine the effectiveness of the potential antagonist. The gene encoding the receptor can be identified by numerous methods known to those of skill in the art, for example, ligand panning and FACS sorting. Coligan et al., Current Protocols in Immun., 1(2): Chapter 5 (1991). Preferably, expression cloning is employed wherein polyadenylated RNA is prepared from a cell responsive to the PRO polypeptide and a cDNA library created from this RNA is divided into pools and used to transfect COS cells or other cells that are not responsive to the PRO polypeptide. Transfected cells that are grown on glass slides are exposed to labeled PRO polypeptide. The PRO polypeptide can be labeled by a variety of means including iodination or inclusion of a recognition site for a site-specific protein kinase. Following fixation and incubation, the slides are subjected to autoradiographic analysis. Positive pools are identified and sub-pools are prepared and re-transfected using an interactive sub-pooling and re-screening process, eventually yielding a



single clone that encodes the putative receptor.

As an alternative approach for receptor identification, labeled PRO polypeptide can be photoaffinity-linked with cell membrane or extract preparations that express the receptor molecule. Cross-linked material is resolved by PAGE and exposed to X-ray film. The labeled complex containing the receptor can be excised, resolved into peptide fragments, and subjected to protein micro-sequencing. The amino acid sequence obtained from micro-sequencing would be used to design a set of degenerate oligonucleotide probes to screen a cDNA library to identify the gene encoding the putative receptor.

In another assay for antagonists, mammalian cells or a membrane preparation expressing the receptor would be incubated with labeled PRO polypeptide in the presence of the candidate compound. The ability of the compound to enhance or block this interaction could then be measured.

More specific examples of potential antagonists include an oligonucleotide that binds to the fusions of immunoglobulin with PRO polypeptide, and, in particular, antibodies including, without limitation, poly- and monoclonal antibodies and antibody fragments, single-chain antibodies, anti-idiotypic antibodies, and chimeric or humanized versions of such antibodies or fragments, as well as human antibodies and antibody fragments. Alternatively, a potential antagonist may be a closely related protein, for example, a mutated form of the PRO polypeptide that recognizes the receptor but imparts no effect, thereby competitively inhibiting the action of the PRO polypeptide.

Another potential PRO polypeptide antagonist is an antisense RNA or DNA construct prepared using antisense technology, where, e.g., an antisense RNA or DNA molecule acts to block directly the translation of mRNA by hybridizing to targeted mRNA and preventing protein translation. Antisense technology can be used to control gene expression through triple-helix formation or antisense DNA or RNA, both of which methods are based on binding of a polynucleotide to DNA or RNA. For example, the 5' coding portion of the polynucleotide sequence, which encodes the mature PRO polypeptides herein, is used to design an antisense RNA oligonucleotide of from about 10 to 40 base pairs in length. A DNA oligonucleotide is designed to be complementary to a region of the gene involved in transcription (triple helix - see Lee et al., Nucl. Acids Res., 6:3073 (1979); Cooney et al., Science, 241: 456 (1988); Dervan et al., Science, 251:1360 (1991)), thereby preventing transcription and the production of the PRO polypeptide. The antisense RNA oligonucleotide hybridizes to the mRNA *in vivo* and blocks translation of the mRNA molecule into the PRO polypeptide (antisense - Okano, Neurochem., 56:560 (1991); Oligodeoxynucleotides as Antisense Inhibitors of Gene Expression (CRC Press: Boca Raton, FL, 1988). The oligonucleotides described above can also be delivered to cells such that the antisense RNA or DNA may be expressed *in vivo* to inhibit production of the PRO polypeptide. When antisense DNA is used, oligodeoxyribonucleotides derived from the translation-initiationsite, e.g., between about -10 and +10 positions of the target gene nucleotide sequence, are preferred.

Potential antagonists include small molecules that bind to the active site, the receptor binding site, or growth factor or other relevant binding site of the PRO polypeptide, thereby blocking the normal biological activity of the PRO polypeptide. Examples of small molecules include, but are not limited to, small peptides or peptide-like molecules, preferably soluble peptides, and synthetic non-peptidyl organic or inorganic compounds.

Ribozymes are enzymatic RNA molecules capable of catalyzing the specific cleavage of RNA. Ribozymes act by sequence-specific hybridization to the complementary target RNA, followed by endonucleolytic cleavage. Specific ribozyme cleavage sites within a potential RNA target can be identified by known techniques. For further details see, e.g., Rossi, Current Biology, 4:469-471 (1994), and PCT publication No. WO 97/33551 (published September 18, 1997).

5 Nucleic acid molecules in triple-helix formation used to inhibit transcription should be single-stranded and composed of deoxynucleotides. The base composition of these oligonucleotides is designed such that it promotes triple-helix formation via Hoogsteen base-pairing rules, which generally require sizeable stretches of purines or pyrimidines on one strand of a duplex. For further details see, e.g., PCT publication No. WO 97/33551, *supra*.

10 These small molecules can be identified by any one or more of the screening assays discussed hereinabove and/or by any other screening techniques well known for those skilled in the art.

PRO189 can be used in assays with W01A6.1 of *C. Elegans*, phosphodiesterases, transporters and proteins which bind to fatty acids, to determine the relative activities of PRO189 against these proteins. The results can be applied accordingly.

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#### F. Anti-PRO Antibodies

The present invention further provides anti-PRO antibodies. Exemplary antibodies include polyclonal, monoclonal, humanized, bispecific, and heteroconjugate antibodies.

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##### 1. Polyclonal Antibodies

The anti-PRO antibodies may comprise polyclonal antibodies. Methods of preparing polyclonal antibodies are known to the skilled artisan. Polyclonal antibodies can be raised in a mammal, for example, by one or more injections of an immunizing agent and, if desired, an adjuvant. Typically, the immunizing agent and/or adjuvant will be injected in the mammal by multiple subcutaneous or intraperitoneal injections. The immunizing agent may include the PRO polypeptide or a fusion protein thereof. It may be useful to conjugate the immunizing agent to a protein known to be immunogenic in the mammal being immunized. Examples of such immunogenic proteins include but are not limited to keyhole limpet hemocyanin, serum albumin, bovine thyroglobulin, and soybean trypsin inhibitor. Examples of adjuvants which may be employed include Freund's complete adjuvant and MPL-TDM adjuvant (monophosphoryl Lipid A, synthetic trehalose dicorynomycolate).  
25 The immunization protocol may be selected by one skilled in the art without undue experimentation.  
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##### 2. Monoclonal Antibodies

The anti-PRO antibodies may, alternatively, be monoclonal antibodies. Monoclonal antibodies may be prepared using hybridoma methods, such as those described by Kohler and Milstein, Nature, 256:495 (1975).  
35 In a hybridoma method, a mouse, hamster, or other appropriate host animal, is typically immunized with an immunizing agent to elicit lymphocytes that produce or are capable of producing antibodies that will specifically bind to the immunizing agent. Alternatively, the lymphocytes may be immunized *in vitro*.

The immunizing agent will typically include the PRO polypeptide or a fusion protein thereof. Generally, either peripheral blood lymphocytes ("PBLs") are used if cells of human origin are desired, or spleen cells or lymph node cells are used if non-human mammalian sources are desired. The lymphocytes are then fused with an immortalized cell line using a suitable fusing agent, such as polyethylene glycol, to form a hybridoma cell [Goding, Monoclonal Antibodies: Principles and Practice, Academic Press, (1986) pp. 59-103].

- 5   Immortalized cell lines are usually transformed mammalian cells, particularly myeloma cells of rodent, bovine and human origin. Usually, rat or mouse myeloma cell lines are employed. The hybridoma cells may be cultured in a suitable culture medium that preferably contains one or more substances that inhibit the growth or survival of the unfused, immortalized cells. For example, if the parental cells lack the enzyme hypoxanthine guanine phosphoribosyl transferase (HGPRT or HPRT), the culture medium for the hybridomas typically will
- 10   include hypoxanthine, aminopterin, and thymidine ("HAT medium"), which substances prevent the growth of HGPRT-deficient cells.

- Preferred immortalized cell lines are those that fuse efficiently, support stable high level expression of antibody by the selected antibody-producing cells, and are sensitive to a medium such as HAT medium. More preferred immortalized cell lines are murine myeloma lines, which can be obtained, for instance, from the Salk
- 15   Institute Cell Distribution Center, San Diego, California and the American Type Culture Collection, Manassas, Virginia. Human myeloma and mouse-human heteromyeloma cell lines also have been described for the production of human monoclonal antibodies [Kozbor, J. Immunol., 133:3001 (1984); Brodeur et al., Monoclonal Antibody Production Techniques and Applications, Marcel Dekker, Inc., New York, (1987) pp. 51-63].

- The culture medium in which the hybridoma cells are cultured can then be assayed for the presence of
- 20   monoclonal antibodies directed against PRO. Preferably, the binding specificity of monoclonal antibodies produced by the hybridoma cells is determined by immunoprecipitation or by an *in vitro* binding assay, such as radioimmunoassay (RIA) or enzyme-linked immunoabsorbent assay (ELISA). Such techniques and assays are known in the art. The binding affinity of the monoclonal antibody can, for example, be determined by the Scatchard analysis of Munson and Pollard, Anal. Biochem., 107:220 (1980).

- 25   After the desired hybridoma cells are identified, the clones may be subcloned by limiting dilution procedures and grown by standard methods [Goding, supra]. Suitable culture media for this purpose include, for example, Dulbecco's Modified Eagle's Medium and RPMI-1640 medium. Alternatively, the hybridoma cells may be grown *in vivo* as ascites in a mammal.

- The monoclonal antibodies secreted by the subclones may be isolated or purified from the culture
- 30   medium or ascites fluid by conventional immunoglobulin purification procedures such as, for example, protein A-Sepharose, hydroxylapatite chromatography, gel electrophoresis, dialysis, or affinity chromatography.

- The monoclonal antibodies may also be made by recombinant DNA methods, such as those described in U.S. Patent No. 4,816,567. DNA encoding the monoclonal antibodies of the invention can be readily isolated and sequenced using conventional procedures (e.g., by using oligonucleotide probes that are capable of binding
- 35   specifically to genes encoding the heavy and light chains of murine antibodies). The hybridoma cells of the invention serve as a preferred source of such DNA. Once isolated, the DNA may be placed into expression vectors, which are then transfected into host cells such as simian COS cells, Chinese hamster ovary (CHO) cells,

or myeloma cells that do not otherwise produce immunoglobulin protein, to obtain the synthesis of monoclonal antibodies in the recombinant host cells. The DNA also may be modified, for example, by substituting the coding sequence for human heavy and light chain constant domains in place of the homologous murine sequences [U.S. Patent No. 4,816,567; Morrison et al., *supra*] or by covalently joining to the immunoglobulin coding sequence all or part of the coding sequence for a non-immunoglobulin polypeptide. Such a non-immunoglobulin polypeptide can be substituted for the constant domains of an antibody of the invention, or can be substituted for the variable domains of one antigen-combining site of an antibody of the invention to create a chimeric bivalent antibody.

The antibodies may be monovalent antibodies. Methods for preparing monovalent antibodies are well known in the art. For example, one method involves recombinant expression of immunoglobulin light chain and modified heavy chain. The heavy chain is truncated generally at any point in the Fc region so as to prevent heavy chain crosslinking. Alternatively, the relevant cysteine residues are substituted with another amino acid residue or are deleted so as to prevent crosslinking.

*In vitro* methods are also suitable for preparing monovalent antibodies. Digestion of antibodies to produce fragments thereof, particularly, Fab fragments, can be accomplished using routine techniques known in the art.

### 3. Human and Humanized Antibodies

The anti-PRO antibodies of the invention may further comprise humanized antibodies or human antibodies. Humanized forms of non-human (e.g., murine) antibodies are chimeric immunoglobulins, immunoglobulin chains or fragments thereof (such as Fv, Fab, Fab', F(ab')<sub>2</sub> or other antigen-binding subsequences of antibodies) which contain minimal sequence derived from non-human immunoglobulin. Humanized antibodies include human immunoglobulins (recipient antibody) in which residues from a complementary determining region (CDR) of the recipient are replaced by residues from a CDR of a non-human species (donor antibody) such as mouse, rat or rabbit having the desired specificity, affinity and capacity. In some instances, Fv framework residues of the human immunoglobulin are replaced by corresponding non-human residues. Humanized antibodies may also comprise residues which are found neither in the recipient antibody nor in the imported CDR or framework sequences. In general, the humanized antibody will comprise substantially all of at least one, and typically two, variable domains, in which all or substantially all of the CDR regions correspond to those of a non-human immunoglobulin and all or substantially all of the FR regions are those of a human immunoglobulin consensus sequence. The humanized antibody optimally also will comprise at least a portion of an immunoglobulin constant region (Fc), typically that of a human immunoglobulin [Jones et al., *Nature*, 321:522-525 (1986); Riechmann et al., *Nature*, 332:323-329 (1988); and Presta, *Curr. Op. Struct. Biol.*, 2:593-596 (1992)].

Methods for humanizing non-human antibodies are well known in the art. Generally, a humanized antibody has one or more amino acid residues introduced into it from a source which is non-human. These non-human amino acid residues are often referred to as "import" residues, which are typically taken from an "import" variable domain. Humanization can be essentially performed following the method of Winter and co-workers

[Jones et al., *Nature*, 321:522-525 (1986); Riechmann et al., *Nature*, 332:323-327 (1988); Verhoeyen et al., *Science*, 239:1534-1536 (1988)], by substituting rodent CDRs or CDR sequences for the corresponding sequences of a human antibody. Accordingly, such "humanized" antibodies are chimeric antibodies (U.S. Patent No. 4,816,567), wherein substantially less than an intact human variable domain has been substituted by the corresponding sequence from a non-human species. In practice, humanized antibodies are typically human antibodies in which some CDR residues and possibly some FR residues are substituted by residues from analogous sites in rodent antibodies.

Human antibodies can also be produced using various techniques known in the art, including phage display libraries [Hoogenboom and Winter, *J. Mol. Biol.*, 227:381 (1991); Marks et al., *J. Mol. Biol.*, 222:581 (1991)]. The techniques of Cole et al. and Boerner et al. are also available for the preparation of human monoclonal antibodies (Cole et al., *Monoclonal Antibodies and Cancer Therapy*, Alan R. Liss, p. 77 (1985) and Boerner et al., *J. Immunol.*, 147(1):86-95 (1991)]. Similarly, human antibodies can be made by introducing of human immunoglobulin loci into transgenic animals, e.g., mice in which the endogenous immunoglobulin genes have been partially or completely inactivated. Upon challenge, human antibody production is observed, which closely resembles that seen in humans in all respects, including gene rearrangement, assembly, and antibody repertoire. This approach is described, for example, in U.S. Patent Nos. 5,545,807; 5,545,806; 5,569,825; 5,625,126; 5,633,425; 5,661,016, and in the following scientific publications: Marks et al., *Bio/Technology* 10, 779-783 (1992); Lonberg et al., *Nature* 368 856-859 (1994); Morrison, *Nature* 368, 812-13 (1994); Fishwild et al., *Nature Biotechnology* 14, 845-51 (1996); Neuberger, *Nature Biotechnology* 14, 826 (1996); Lonberg and Huszar, *Intern. Rev. Immunol.* 13 65-93 (1995).

#### 4. Bispecific Antibodies

Bispecific antibodies are monoclonal, preferably human or humanized, antibodies that have binding specificities for at least two different antigens. In the present case, one of the binding specificities is for the PRO, the other one is for any other antigen, and preferably for a cell-surface protein or receptor or receptor subunit.

Methods for making bispecific antibodies are known in the art. Traditionally, the recombinant production of bispecific antibodies is based on the co-expression of two immunoglobulin heavy-chain/light-chain pairs, where the two heavy chains have different specificities [Milstein and Cuello, *Nature*, 305:537-539 (1983)]. Because of the random assortment of immunoglobulin heavy and light chains, these hybridomas (quadromas) produce a potential mixture of ten different antibody molecules, of which only one has the correct bispecific structure. The purification of the correct molecule is usually accomplished by affinity chromatography steps. Similar procedures are disclosed in WO 93/08829, published 13 May 1993, and in Traunecker et al., *EMBO J.*, 10:3655-3659 (1991).

Antibody variable domains with the desired binding specificities (antibody-antigen combining sites) can be fused to immunoglobulin constant domain sequences. The fusion preferably is with an immunoglobulin heavy-chain constant domain, comprising at least part of the hinge, CH2, and CH3 regions. It is preferred to have the first heavy-chain constant region (CH1) containing the site necessary for light-chain binding present in

at least one of the fusions. DNAs encoding the immunoglobulin heavy-chain fusions and, if desired, the immunoglobulin light chain, are inserted into separate expression vectors, and are co-transfected into a suitable host organism. For further details of generating bispecific antibodies see, for example, Suresh et al., Methods in Enzymology, 121:210 (1986).

5 According to another approach described in WO 96/27011, the interface between a pair of antibody molecules can be engineered to maximize the percentage of heterodimers which are recovered from recombinant cell culture. The preferred interface comprises at least a part of the CH3 region of an antibody constant domain. In this method, one or more small amino acid side chains from the interface of the first antibody molecule are replaced with larger side chains (e.g. tyrosine or tryptophan). Compensatory "cavities" of identical or similar size to the large side chain(s) are created on the interface of the second antibody molecule by replacing large amino acid side chains with smaller ones (e.g. alanine or threonine). This provides a mechanism for increasing the yield of the heterodimer over other unwanted end-products such as homodimers.

Bispecific antibodies can be prepared as full length antibodies or antibody fragments (e.g. F(ab')<sub>2</sub> bispecific antibodies). Techniques for generating bispecific antibodies from antibody fragments have been described in the literature. For example, bispecific antibodies can be prepared using chemical linkage. Brennan et al., Science 229:81 (1985) describe a procedure wherein intact antibodies are proteolytically cleaved to generate F(ab')<sub>2</sub> fragments. These fragments are reduced in the presence of the dithiol complexing agent sodium arsenite to stabilize vicinal dithiols and prevent intermolecular disulfide formation. The Fab' fragments generated are then converted to thionitrobenzoate (TNB) derivatives. One of the Fab'-TNB derivatives is then reconverted to the Fab'-thiol by reduction with mercaptoethylamine and is mixed with an equimolar amount of the other Fab'-TNB derivative to form the bispecific antibody. The bispecific antibodies produced can be used as agents for the selective immobilization of enzymes.

Fab' fragments may be directly recovered from *E. coli* and chemically coupled to form bispecific antibodies. Shalaby et al., J. Exp. Med. 175:217-225 (1992) describe the production of a fully humanized bispecific antibody F(ab')<sub>2</sub> molecule. Each Fab' fragment was separately secreted from *E. coli* and subjected to directed chemical coupling *in vitro* to form the bispecific antibody. The bispecific antibody thus formed was able to bind to cells overexpressing the ErbB2 receptor and normal human T cells, as well as trigger the lytic activity of human cytotoxic lymphocytes against human breast tumor targets.

Various technique for making and isolating bispecific antibody fragments directly from recombinant cell culture have also been described. For example, bispecific antibodies have been produced using leucine zippers. Kostelny et al., J. Immunol. 148(5):1547-1553 (1992). The leucine zipper peptides from the Fos and Jun proteins were linked to the Fab' portions of two different antibodies by gene fusion. The antibody homodimers were reduced at the hinge region to form monomers and then re-oxidized to form the antibody heterodimers. This method can also be utilized for the production of antibody homodimers. The "diabody" technology described by Hollinger et al., Proc. Natl. Acad. Sci. USA 90:6444-6448 (1993) has provided an alternative mechanism for making bispecific antibody fragments. The fragments comprise a heavy-chain variable domain (V<sub>H</sub>) connected to a light-chain variable domain (V<sub>L</sub>) by a linker which is too short to allow pairing between the two domains on the same chain. Accordingly, the V<sub>H</sub> and V<sub>L</sub> domains of one fragment are forced to pair with

the complementary  $V_L$  and  $V_H$  domains of another fragment, thereby forming two antigen-binding sites. Another strategy for making bispecific antibody fragments by the use of single-chain Fv (sFv) dimers has also been reported. See, Gruber *et al.*, *J. Immunol.* 152:5368 (1994).

Antibodies with more than two valencies are contemplated. For example, trispecific antibodies can be prepared. Tutt *et al.*, *J. Immunol.* 147:60 (1991).

- 5 Exemplary bispecific antibodies may bind to two different epitopes on a given PRO polypeptide herein. Alternatively, an anti-PRO polypeptide arm may be combined with an arm which binds to a triggering molecule on a leukocyte such as a T-cell receptor molecule (e.g. CD2, CD3, CD28, or B7), or Fc receptors for IgG (FcγR), such as FcγRI (CD64), FcγRII (CD32) and FcγRIII (CD16) so as to focus cellular defense mechanisms to the cell expressing the particular PRO polypeptide. Bispecific antibodies may also be used to localize  
10 cytotoxic agents to cells which express a particular PRO polypeptide. These antibodies possess a PRO-binding arm and an arm which binds a cytotoxic agent or a radionuclide chelator, such as EOTUBE, DPTA, DOTA, or TETA. Another bispecific antibody of interest binds the PRO polypeptide and further binds tissue factor (TF).

15 5. Heteroconjugate Antibodies

- Heteroconjugate antibodies are also within the scope of the present invention. Heteroconjugate antibodies are composed of two covalently joined antibodies. Such antibodies have, for example, been proposed to target immune system cells to unwanted cells [U.S. Patent No. 4,676,980], and for treatment of HIV infection [WO 91/00360; WO 92/200373; EP 03089]. It is contemplated that the antibodies may be prepared *in vitro*  
20 using known methods in synthetic protein chemistry, including those involving crosslinking agents. For example, immunotoxins may be constructed using a disulfide exchange reaction or by forming a thioether bond. Examples of suitable reagents for this purpose include iminothiolate and methyl-4-mercaptobutyrimidate and those disclosed, for example, in U.S. Patent No. 4,676,980.

25 6. Effector Function Engineering

- It may be desirable to modify the antibody of the invention with respect to effector function, so as to enhance, e.g., the effectiveness of the antibody in treating cancer. For example, cysteine residue(s) may be introduced into the Fc region, thereby allowing interchain disulfide bond formation in this region. The homodimeric antibody thus generated may have improved internalization capability and/or increased  
30 complement-mediated cell killing and antibody-dependent cellular cytotoxicity (ADCC). See Caron *et al.*, *J. Exp Med.*, 176: 1191-1195 (1992) and Shopes, *J. Immunol.*, 148: 2918-2922 (1992). Homodimeric antibodies with enhanced anti-tumor activity may also be prepared using heterobifunctional cross-linkers as described in Wolff *et al.* *Cancer Research*, 53: 2560-2565 (1993). Alternatively, an antibody can be engineered that has dual Fc regions and may thereby have enhanced complement lysis and ADCC capabilities. See Stevenson *et al.*, *Anti-Cancer Drug Design*, 3: 219-230 (1989).

### 7. Immunoconjugates

The invention also pertains to immunoconjugates comprising an antibody conjugated to a cytotoxic agent such as a chemotherapeutic agent, toxin (*e.g.*, an enzymatically active toxin of bacterial, fungal, plant, or animal origin, or fragments thereof), or a radioactive isotope (*i.e.*, a radioconjugate).

Chemotherapeutic agents useful in the generation of such immunoconjugates have been described above.

- 5 Enzymatically active toxins and fragments thereof that can be used include diphtheria A chain, nonbinding active fragments of diphtheria toxin, exotoxin A chain (from *Pseudomonas aeruginosa*), ricin A chain, abrin A chain, modeccin A chain, alpha-sarcin, *Aleurites fordii* proteins, dianthin proteins, *Phytolacca americana* proteins (PAPI, PAPII, and PAP-S), momordica charantia inhibitor, curcin, crotin, sapaonaria officinalis inhibitor, gelonin, mitogellin, restrictocin, phenomycin, enomycin, and the tricothecenes. A variety of radionuclides are  
10 available for the production of radioconjugated antibodies. Examples include  $^{212}\text{Bi}$ ,  $^{131}\text{I}$ ,  $^{131}\text{In}$ ,  $^{90}\text{Y}$ , and  $^{186}\text{Re}$ .

- Conjugates of the antibody and cytotoxic agent are made using a variety of bifunctional protein-coupling agents such as N-succinimidyl-3-(2-pyridyldithiol) propionate (SPDP), iminothiolane (IT), bifunctional derivatives of imidoesters (such as dimethyl adipimidate HCL), active esters (such as disuccinimidyl suberate), aldehydes (such as glutaraldehyde), bis-azido compounds (such as bis (p-azidobenzoyl) hexanediamine), bis-  
15 diazonium derivatives (such as bis-(p-diazoniumbenzoyl)-ethylenediamine), diisocyanates (such as tolyene 2,6-diisocyanate), and bis-active fluorine compounds (such as 1,5-difluoro-2,4-dinitrobenzene). For example, a ricin immunotoxin can be prepared as described in Vitetta *et al.*, Science, **238**: 1098 (1987). Carbon-14-labeled 1-isothiocyanatobenzyl-3-methyldiethylene triaminepentaacetic acid (MX-DTPA) is an exemplary chelating agent for conjugation of radionucleotide to the antibody. See WO94/11026.

- 20 In another embodiment, the antibody may be conjugated to a "receptor" (such streptavidin) for utilization in tumor pretargeting wherein the antibody-receptor conjugate is administered to the patient, followed by removal of unbound conjugate from the circulation using a clearing agent and then administration of a "ligand" (*e.g.*, avidin) that is conjugated to a cytotoxic agent (*e.g.*, a radionucleotide).

### 25 8. Immunoliposomes

- The antibodies disclosed herein may also be formulated as immunoliposomes. Liposomes containing the antibody are prepared by methods known in the art, such as described in Epstein *et al.*, Proc. Natl. Acad. Sci. USA, **82**: 3688 (1985); Hwang *et al.*, Proc. Natl. Acad. Sci. USA, **77**: 4030 (1980); and U.S. Pat. Nos. 4,485,045 and 4,544,545. Liposomes with enhanced circulation time are disclosed in U.S. Patent No.  
30 5,013,556.

- Particularly useful liposomes can be generated by the reverse-phase evaporation method with a lipid composition comprising phosphatidylcholine, cholesterol, and PEG-derivatized phosphatidylethanolamine (PEG-PE). Liposomes are extruded through filters of defined pore size to yield liposomes with the desired diameter. Fab' fragments of the antibody of the present invention can be conjugated to the liposomes as described in Martin  
35 *et al.*, J. Biol. Chem., **257**: 286-288 (1982) via a disulfide-interchange reaction. A chemotherapeutic agent (such as Doxorubicin) is optionally contained within the liposome. See Gabizon *et al.*, J. National Cancer Inst., **81**(19): 1484 (1989).



#### 9. Pharmaceutical Compositions of Antibodies

Antibodies specifically binding a PRO polypeptide identified herein, as well as other molecules identified by the screening assays disclosed hereinbefore, can be administered for the treatment of various disorders in the form of pharmaceutical compositions.

If the PRO polypeptide is intracellular and whole antibodies are used as inhibitors, internalizing antibodies are preferred. However, lipofections or liposomes can also be used to deliver the antibody, or an antibody fragment, into cells. Where antibody fragments are used, the smallest inhibitory fragment that specifically binds to the binding domain of the target protein is preferred. For example, based upon the variable-region sequences of an antibody, peptide molecules can be designed that retain the ability to bind the target protein sequence. Such peptides can be synthesized chemically and/or produced by recombinant DNA technology. See, *e.g.*, Marasco *et al.*, Proc. Natl. Acad. Sci. USA, 90: 7889-7893 (1993). The formulation herein may also contain more than one active compound as necessary for the particular indication being treated, preferably those with complementary activities that do not adversely affect each other. Alternatively, or in addition, the composition may comprise an agent that enhances its function, such as, for example, a cytotoxic agent, cytokine, chemotherapeutic agent, or growth-inhibitory agent. Such molecules are suitably present in combination in amounts that are effective for the purpose intended.

The active ingredients may also be entrapped in microcapsules prepared, for example, by coacervation techniques or by interfacial polymerization, for example, hydroxymethylcellulose or gelatin-microcapsules and poly-(methylmethacrylate) microcapsules, respectively, in colloidal drug delivery systems (for example, liposomes, albumin microspheres, microemulsions, nano-particles, and nanocapsules) or in macroemulsions. Such techniques are disclosed in Remington's Pharmaceutical Sciences, *supra*.

The formulations to be used for *in vivo* administration must be sterile. This is readily accomplished by filtration through sterile filtration membranes.

Sustained-release preparations may be prepared. Suitable examples of sustained-release preparations include semipermeable matrices of solid hydrophobic polymers containing the antibody, which matrices are in the form of shaped articles, *e.g.*, films, or microcapsules. Examples of sustained-release matrices include polyesters, hydrogels (for example, poly(2-hydroxyethyl-methacrylate), or poly(vinylalcohol)), polylactides (U.S. Pat. No. 3,773,919), copolymers of L-glutamic acid and  $\gamma$  ethyl-L-glutamate, non-degradable ethylene-vinyl acetate, degradable lactic acid-glycolic acid copolymers such as the LUPRON DEPOT™ (injectable microspheres composed of lactic acid-glycolic acid copolymer and leuprolide acetate), and poly-D-(-)-3-hydroxybutyric acid. While polymers such as ethylene-vinyl acetate and lactic acid-glycolic acid enable release of molecules for over 100 days, certain hydrogels release proteins for shorter time periods. When encapsulated antibodies remain in the body for a long time, they may denature or aggregate as a result of exposure to moisture at 37°C, resulting in a loss of biological activity and possible changes in immunogenicity. Rational strategies can be devised for stabilization depending on the mechanism involved. For example, if the aggregation mechanism is discovered to be intermolecular S-S bond formation through thio-disulfide interchange, stabilization may be achieved by modifying sulfhydryl residues, lyophilizing from acidic solutions, controlling moisture content, using appropriate additives, and developing specific polymer matrix compositions.

G. Uses for anti-PRO Antibodies

The anti-PRO antibodies of the invention have various utilities. For example, anti-PRO antibodies may be used in diagnostic assays for PRO, *e.g.*, detecting its expression in specific cells, tissues, or serum. Various diagnostic assay techniques known in the art may be used, such as competitive binding assays, direct or indirect sandwich assays and immunoprecipitation assays conducted in either heterogeneous or homogeneous phases

5 [Zola, Monoclonal Antibodies: A Manual of Techniques, CRC Press, Inc. (1987) pp. 147-158]. The antibodies used in the diagnostic assays can be labeled with a detectable moiety. The detectable moiety should be capable of producing, either directly or indirectly, a detectable signal. For example, the detectable moiety may be a radioisotope, such as  $^3\text{H}$ ,  $^{14}\text{C}$ ,  $^{32}\text{P}$ ,  $^{35}\text{S}$ , or  $^{125}\text{I}$ , a fluorescent or chemiluminescent compound, such as fluorescein isothiocyanate, rhodamine, or luciferin, or an enzyme, such as alkaline phosphatase, beta-galactosidase or

10 horseradish peroxidase. Any method known in the art for conjugating the antibody to the detectable moiety may be employed, including those methods described by Hunter et al., Nature, 144:945 (1962); David et al., Biochemistry, 13:1014 (1974); Pain et al., J. Immunol. Meth., 40:219 (1981); and Nygren, J. Histochem. and Cytochem., 30:407 (1982).

Anti-PRO antibodies also are useful for the affinity purification of PRO from recombinant cell culture

15 or natural sources. In this process, the antibodies against PRO are immobilized on a suitable support, such as Sephadex resin or filter paper, using methods well known in the art. The immobilized antibody then is contacted with a sample containing the PRO to be purified, and thereafter the support is washed with a suitable solvent that will remove substantially all the material in the sample except the PRO, which is bound to the immobilized antibody. Finally, the support is washed with another suitable solvent that will release the PRO from the

20 antibody.

The following examples are offered for illustrative purposes only, and are not intended to limit the scope of the present invention in any way.

All patent and literature references cited in the present specification are hereby incorporated by reference in their entirety.

25

EXAMPLES

Commercially available reagents referred to in the examples were used according to manufacturer's instructions unless otherwise indicated. The source of those cells identified in the following examples, and throughout the specification, by ATCC accession numbers is the American Type Culture Collection, Manassas,

30 VA.

EXAMPLE 1: Extracellular Domain Homology Screening to Identify Novel Polypeptides and cDNA Encoding Therefor

The extracellular domain (ECD) sequences (including the secretion signal sequence, if any) from about

35 950 known secreted proteins from the Swiss-Prot public database were used to search EST databases. The EST databases included public databases (*e.g.*, Dayhoff, GenBank), and proprietary databases (*e.g.* LIFESEQ™, Incyte Pharmaceuticals, Palo Alto, CA). The search was performed using the computer program WU-BLAST-2

(Altschul et al., Methods in Enzymology 266:460-480 (1996)) as a comparison of the ECD protein sequences to a 6 frame translation of the EST sequences. Those comparisons with a Blast score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into consensus DNA sequences with the program "phrap" (Phil Green, University of Washington, Seattle, WA).

5 Using this extracellular domain homology screen, consensus DNA sequences were assembled relative to the other identified EST sequences using phrap. In addition, the consensus DNA sequences obtained were often (but not always) extended using repeated cycles of WU-BLAST-2 and phrap to extend the consensus sequence as far as possible using the sources of EST sequences discussed above.

Based upon the consensus sequences obtained as described above, oligonucleotides were then synthesized and used to identify by PCR a cDNA library that contained the sequence of interest and for use as probes to isolate a clone of the full-length coding sequence for a PRO polypeptide. Forward and reverse PCR primers generally range from 20 to 30 nucleotides and are often designed to give a PCR product of about 100-1000 bp in length. The probe sequences are typically 40-55 bp in length. In some cases, additional oligonucleotides are synthesized when the consensus sequence is greater than about 1-1.5kbp. In order to screen several libraries for a full-length clone, DNA from the libraries was screened by PCR amplification, as per  
10 Ausubel et al., Current Protocols in Molecular Biology, with the PCR primer pair. A positive library was then used to isolate clones encoding the gene of interest using the probe oligonucleotide and one of the primer pairs.

The cDNA libraries used to isolate the cDNA clones were constructed by standard methods using commercially available reagents such as those from Invitrogen, San Diego, CA. The cDNA was primed with oligo dT containing a NotI site, linked with blunt to SalI hemikinased adaptors, cleaved with NotI, sized  
20 appropriately by gel electrophoresis, and cloned in a defined orientation into a suitable cloning vector (such as pRKB or pRKD; pRK5B is a precursor of pRK5D that does not contain the SfiI site; see, Holmes et al., Science, 253:1278-1280 (1991)) in the unique XhoI and NotI sites.

#### EXAMPLE 2: Isolation of cDNA clones by Amylase Screening

##### 25 1. Preparation of oligo dT primed cDNA library

mRNA was isolated from a human tissue of interest using reagents and protocols from Invitrogen, San Diego, CA (Fast Track 2). This RNA was used to generate an oligo dT primed cDNA library in the vector pRK5D using reagents and protocols from Life Technologies, Gaithersburg, MD (Super Script Plasmid System). In this procedure, the double stranded cDNA was sized to greater than 1000 bp and the SalI/NotI linked cDNA  
30 was cloned into XhoI/NotI cleaved vector. pRK5D is a cloning vector that has an sp6 transcription initiation site followed by an SfiI restriction enzyme site preceding the XhoI/NotI cDNA cloning sites.

##### 2. Preparation of random primed cDNA library

A secondary cDNA library was generated in order to preferentially represent the 5' ends of the primary  
35 cDNA clones. Sp6 RNA was generated from the primary library (described above), and this RNA was used to generate a random primed cDNA library in the vector pSST-AMY.0 using reagents and protocols from Life Technologies (Super Script Plasmid System, referenced above). In this procedure the double stranded cDNA

was sized to 500-1000 bp, linked with blunt to NotI adaptors, cleaved with SfiI, and cloned into SfiI/NotI cleaved vector. pSST-AMY.0 is a cloning vector that has a yeast alcohol dehydrogenase promoter preceding the cDNA cloning sites and the mouse amylase sequence (the mature sequence without the secretion signal) followed by the yeast alcohol dehydrogenase terminator, after the cloning sites. Thus, cDNAs cloned into this vector that are fused in frame with amylase sequence will lead to the secretion of amylase from appropriately transfected yeast colonies.

### 3. Transformation and Detection

DNA from the library described in paragraph 2 above was chilled on ice to which was added electrocompetent DH10B bacteria (Life Technologies, 20 ml). The bacteria and vector mixture was then electroporated as recommended by the manufacturer. Subsequently, SOC media (Life Technologies, 1 ml) was added and the mixture was incubated at 37°C for 30 minutes. The transformants were then plated onto 20 standard 150 mm LB plates containing ampicillin and incubated for 16 hours (37°C). Positive colonies were scraped off the plates and the DNA was isolated from the bacterial pellet using standard protocols, e.g. CsCl-gradient. The purified DNA was then carried on to the yeast protocols below.

The yeast methods were divided into three categories: (1) Transformation of yeast with the plasmid/cDNA combined vector; (2) Detection and isolation of yeast clones secreting amylase; and (3) PCR amplification of the insert directly from the yeast colony and purification of the DNA for sequencing and further analysis.

The yeast strain used was HD56-5A (ATCC-90785). This strain has the following genotype: MAT alpha, ura3-52, leu2-3, leu2-112, his3-11, his3-15, MAL<sup>+</sup>, SUC<sup>+</sup>, GAL<sup>+</sup>. Preferably, yeast mutants can be employed that have deficient post-translational pathways. Such mutants may have translocation deficient alleles in *sec71*, *sec72*, *sec62*, with truncated *sec71* being most preferred. Alternatively, antagonists (including antisense nucleotides and/or ligands) which interfere with the normal operation of these genes, other proteins implicated in this post translation pathway (e.g., SEC61p, SEC72p, SEC62p, SEC63p, TDJ1p or SSA1p-4p) or the complex formation of these proteins may also be preferably employed in combination with the amylase-expressing yeast.

Transformation was performed based on the protocol outlined by Gietz et al., Nucl. Acid. Res., 20:1425 (1992). Transformed cells were then inoculated from agar into YEPD complex media broth (100 ml) and grown overnight at 30°C. The YEPD broth was prepared as described in Kaiser et al., Methods in Yeast Genetics, Cold Spring Harbor Press, Cold Spring Harbor, NY, p. 207 (1994). The overnight culture was then diluted to about  $2 \times 10^6$  cells/ml (approx. OD<sub>600</sub>=0.1) into fresh YEPD broth (500 ml) and regrown to  $1 \times 10^7$  cells/ml (approx. OD<sub>600</sub>=0.4-0.5).

The cells were then harvested and prepared for transformation by transfer into GS3 rotor bottles in a Sorval GS3 rotor at 5,000 rpm for 5 minutes, the supernatant discarded, and then resuspended into sterile water, and centrifuged again in 50 ml falcon tubes at 3,500 rpm in a Beckman GS-6KR centrifuge. The supernatant was discarded and the cells were subsequently washed with LiAc/TE (10 ml, 10 mM Tris-HCl, 1 mM EDTA pH 7.5, 100 mM Li<sub>2</sub>OOCCH<sub>3</sub>), and resuspended into LiAc/TE (2.5 ml).

Transformation took place by mixing the prepared cells (100  $\mu$ l) with freshly denatured single stranded salmon testes DNA (Lofstrand Labs, Gaithersburg, MD) and transforming DNA (1  $\mu$ g, vol. < 10  $\mu$ l) in microfuge tubes. The mixture was mixed briefly by vortexing, then 40% PEG/TE (600  $\mu$ l, 40% polyethylene glycol-4000, 10 mM Tris-HCl, 1 mM EDTA, 100 mM Li<sub>2</sub>OOCCH<sub>3</sub>, pH 7.5) was added. This mixture was gently mixed and incubated at 30°C while agitating for 30 minutes. The cells were then heat shocked at 42°C for 15 minutes, and the reaction vessel centrifuged in a microfuge at 12,000 rpm for 5-10 seconds, decanted and resuspended into TE (500  $\mu$ l, 10 mM Tris-HCl, 1 mM EDTA pH 7.5) followed by recentrifugation. The cells were then diluted into TE (1 ml) and aliquots (200  $\mu$ l) were spread onto the selective media previously prepared in 150 mm growth plates (VWR).

Alternatively, instead of multiple small reactions, the transformation was performed using a single, large scale reaction, wherein reagent amounts were scaled up accordingly.

The selective media used was a synthetic complete dextrose agar lacking uracil (SCD-Ura) prepared as described in Kaiser et al., Methods in Yeast Genetics, Cold Spring Harbor Press, Cold Spring Harbor, NY, p. 208-210 (1994). Transformants were grown at 30°C for 2-3 days.

The detection of colonies secreting amylase was performed by including red starch in the selective growth media. Starch was coupled to the red dye (Reactive Red-120, Sigma) as per the procedure described by Biely et al., Anal. Biochem., 172:176-179 (1988). The coupled starch was incorporated into the SCD-Ura agar plates at a final concentration of 0.15% (w/v), and was buffered with potassium phosphate to a pH of 7.0 (50-100 mM final concentration).

The positive colonies were picked and streaked across fresh selective media (onto 150 mm plates) in order to obtain well isolated and identifiable single colonies. Well isolated single colonies positive for amylase secretion were detected by direct incorporation of red starch into buffered SCD-Ura agar. Positive colonies were determined by their ability to break down starch resulting in a clear halo around the positive colony visualized directly.

#### 25 4. Isolation of DNA by PCR Amplification

When a positive colony was isolated, a portion of it was picked by a toothpick and diluted into sterile water (30  $\mu$ l) in a 96 well plate. At this time, the positive colonies were either frozen and stored for subsequent analysis or immediately amplified. An aliquot of cells (5  $\mu$ l) was used as a template for the PCR reaction in a 25  $\mu$ l volume containing: 0.5  $\mu$ l Klentaq (Clontech, Palo Alto, CA); 4.0  $\mu$ l 10 mM dNTP's (Perkin Elmer-Cetus); 2.5  $\mu$ l Kentaq buffer (Clontech); 0.25  $\mu$ l forward oligo 1; 0.25  $\mu$ l reverse oligo 2; 12.5  $\mu$ l distilled water. The sequence of the forward oligonucleotide 1 was:

5'-TGTAACGACGCGCCAGTTAAATAGACCTGCAATTATTAATCT-3' (SEQ ID NO:3)

The sequence of reverse oligonucleotide 2 was:

5'-CAGGAAACAGCTATGACCACCTGCACACCTGCAAATCCATT-3' (SEQ ID NO:4)

35 PCR was then performed as follows:

- a. Denature 92°C, 5 minutes
- b. 3 cycles of: Denature 92°C, 30 seconds

		Anneal	59°C,	30 seconds
		Extend	72°C,	60 seconds
5	c.	3 cycles of:		
		Denature	92°C,	30 seconds
		Anneal	57°C,	30 seconds
		Extend	72°C,	60 seconds
	d.	25 cycles of:		
		Denature	92°C,	30 seconds
		Anneal	55°C,	30 seconds
10		Extend	72°C,	60 seconds
	e.	Hold	4°C	

The underlined regions of the oligonucleotides annealed to the ADH promoter region and the amylase region, respectively, and amplified a 307 bp region from vector pSST-AMY.0 when no insert was present. Typically, the first 18 nucleotides of the 5' end of these oligonucleotides contained annealing sites for the sequencing primers. Thus, the total product of the PCR reaction from an empty vector was 343 bp. However, signal sequence-fused cDNA resulted in considerably longer nucleotide sequences.

Following the PCR, an aliquot of the reaction (5 µl) was examined by agarose gel electrophoresis in a 1% agarose gel using a Tris-Borate-EDTA (TBE) buffering system as described by Sambrook et al., *supra*. Clones resulting in a single strong PCR product larger than 400 bp were further analyzed by DNA sequencing after purification with a 96 Qiaquick PCR clean-up column (Qiagen Inc., Chatsworth, CA).

#### EXAMPLE 3: Isolation of cDNA Clones Using Signal Algorithm Analysis

Various polypeptide-encoding nucleic acid sequences were identified by applying a proprietary signal sequence finding algorithm developed by Genentech, Inc. (South San Francisco, CA) upon ESTs as well as clustered and assembled EST fragments from public (e.g., GenBank) and/or private (LIFESEQ®, Incyte Pharmaceuticals, Inc., Palo Alto, CA) databases. The signal sequence algorithm computes a secretion signal score based on the character of the DNA nucleotides surrounding the first and optionally the second methionine codon(s) (ATG) at the 5'-end of the sequence or sequence fragment under consideration. The nucleotides following the first ATG must code for at least 35 unambiguous amino acids without any stop codons. If the first ATG has the required amino acids, the second is not examined. If neither meets the requirement, the candidate sequence is not scored. In order to determine whether the EST sequence contains an authentic signal sequence, the DNA and corresponding amino acid sequences surrounding the ATG codon are scored using a set of seven sensors (evaluation parameters) known to be associated with secretion signals. Use of this algorithm resulted in the identification of numerous polypeptide-encoding nucleic acid sequences.

#### EXAMPLE 4: Isolation of cDNA clones Encoding Human PRO281

In order to obtain a cDNA clone encoding PRO281, methods described in Klein et al., *Proc. Natl. Acad. Sci. USA* 93:7108-7113 (1996) were employed with the following modifications. Yeast transformation was performed with limiting amounts of transforming DNA in order to reduce the number of multiple transformed yeast cells. Instead of plasmid isolation from the yeast followed by transformation of *E. coli* as

described in Klein et al., *supra*, PCR analysis was performed on single yeast colonies. PCR primers employed were bipartite in order to amplify the insert and a small portion of the invertase gene (allowing to determine that the insert was in frame with invertase) and to add on universal sequencing primer sites.

An invertase library was transformed into yeast and positives were selected on sucrose plates. Positive clones were re-tested and PCR products were sequenced. The sequence of one clone, PRO281, was determined to contain a signal peptide coding sequence. Oligonucleotide primers and probes were designed using the nucleotide sequence of PRO281. A full length plasmid library of cDNAs from human umbilical vein endothelium tissue was titrated and approximately 100,000 cfu were plated in 192 pools of 500 cfu/pool into 96-well round bottom plates. The plates were sealed and pools were grown overnight at 37°C with shaking (200rpm). PCR was performed on the individual cultures using primers. Agarose gel electrophoresis was performed and positive wells were identified by visualization of a band of the expected size. Individual positive clones were obtained by colony lift followed by hybridization with <sup>32</sup>P-labeled oligonucleotide. These clones were characterized by PCR, restriction digest, and southern blot analyses.

A full length clone was identified that contained a single open reading frame with an apparent translational initiation site at nucleotide positions 80-82, and a stop signal at nucleotide positions 1115-1117 (Figure 1, SEQ ID NO:1). The predicted polypeptide precursor is 345 amino acids long, has a calculated molecular weight of approximately 37,205 daltons and an estimated pI of approximately 10.15. Analysis of the full-length PRO281 sequence shown in Figure 2 (SEQ ID NO:2) evidences the presence of the following: a signal peptide from about amino acid 1 to about amino acid 14, multiple transmembrane domains from about amino acid position 83 to about amino acid position 105, from about amino acid position 126 to about amino acid position 146, from about amino acid position 158 to about amino acid position 177, from about amino acid position 197 to about amino acid position 216, from about amino acid position 218 to about amino acid position 238, from about amino acid position 245 to about amino acid position 265, and from about amino acid position 271 to about amino acid position 290 and an amino acid sequence block having homology to G-protein coupled receptor proteins from about amino acid 115 to about amino acid 155. Clone UNQ244 (DNA16422-1209) has been deposited with ATCC on June 2, 1998 and is assigned ATCC deposit no. 209929.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST-2 sequence alignment analysis of the full-length sequence shown in Figure 2 (SEQ ID NO:2), evidenced significant homology between the PRO281 amino acid sequence and the following Dayhoff sequences: H64634, AF033095\_1, B64815, YBHL\_ECOLI, EMEQUTR\_1, AF064763\_3, S53708, A69253, AF035413\_12 and S63281.

#### EXAMPLE 5: Isolation of cDNA clones Encoding Human PRO276

In order to obtain a cDNA clone encoding PRO276, methods described in Klein et al., *PNAS*, 93:7108-7113 (1996) were employed with the following modifications. Yeast transformation was performed with limiting amounts of transforming DNA in order to reduce the number of multiple transformed yeast cells. Instead of plasmid isolation from the yeast followed by transformation of *E. coli* as described in Klein et al., *supra*, PCR analysis was performed on single yeast colonies. PCR primers employed were bipartite in order to amplify the

insert and a small portion of the invertase gene (allowing to determine that the insert was in frame with invertase) and to add on universal sequencing primer sites.

An invertase library was transformed into yeast and positives were selected on sucrose plates. Positive clones were re-tested and PCR products were sequenced. The sequence of one clone, PRO276, was determined to contain a signal peptide coding sequence. Oligonucleotide primers and probes were designed using the nucleotide sequence of PRO276. A full length plasmid library of cDNAs from human fetal liver cells was titrated and approximately 100,000 cfu were plated in 192 pools of 500 cfu/pool into 96-well round bottom plates. The plates were sealed and pools were grown overnight at 37 C with shaking (200rpm). PCR was performed on the individual cultures using primers. Agarose gel electrophoresis was performed and positive wells were identified by visualization of a band of the expected size. Individual positive clones were obtained by colony lift followed by hybridization with <sup>32</sup>P-labeled oligonucleotide. These clones were characterized by PCR, restriction digest, and southern blot analyses.

A full length clone was identified that contained a single open reading frame with an apparent translational initiation site at nucleotide positions 180-182 and a stop signal at nucleotide positions 933-935 (Figure 3; SEQ ID NO:5). The predicted polypeptide precursor is 251 amino acids long has a calculated molecular weight of approximately 28,801 daltons and an estimated pI of approximately 9.58. The transmembrane domains are approximately at amino acids 98-116 and 152-172 of the sequence shown in Figure 4 (SEQ ID NO:6). Clone DNA16435-1208 (UNQ243) has been deposited with the ATCC and is assigned ATCC deposit no. 209930.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST-2 sequence alignment analysis of the full-length sequence shown in Figure 4 (SEQ ID NO:6), revealed some sequence identity between the PRO276 amino acid sequence and the following Dayhoff sequences: CEG25D7\_2, ATT8O5\_2, S69696, GRHR\_RAT, NPCBAABCD\_3, AB013149\_1, P\_R85942 and AP000006\_5.

#### EXAMPLE 6: Isolation of cDNA clones Encoding Human PRO189

A clone designated herein as DNA14187 was isolated as described in Example 2 above from a human retina tissue library. The DNA14187 sequence is shown in Figure 7 (SEQ ID NO:9). Based on the DNA14187 sequence shown in Figure 7 (SEQ ID NO:9), oligonucleotides were synthesized: 1) to identify by PCR a cDNA library that contained the sequence of interest, and 2) for use as probes to isolate a clone of the full-length coding sequence for PRO189. Forward and reverse PCR primers generally range from 20 to 30 nucleotides and are often designed to give a PCR product of about 100-1000 bp in length. The probe sequences are typically 40-55 bp in length. In order to screen several libraries for a full-length clone, DNA from the libraries was screened by PCR amplification, as per Ausubel et al., Current Protocols in Molecular Biology, with the PCR primer pair. A positive library was then used to isolate clones encoding the gene of interest using the probe oligonucleotide and one of the primer pairs.

A pair of PCR primers (forward and reverse) were synthesized:

forward PCR primer 5'-TTGACCTATACAGAGATTCATC-3' (SEQ ID NO:10); and  
reverse PCR primer 5'-CTAAGAACTTCCCTCAGGATTTT-3' (SEQ ID NO:11).



Additionally, a synthetic oligonucleotide hybridization probe was constructed from the DNA14187 sequence which had the following nucleotide sequence:

hybridization probe

5'-ATGAAGATCAATTTCAAGAAGCATGCACTTCTCCTCTTGC-3' (SEQ ID NO:12).

In order to screen several libraries for a source of a full-length clone, DNA from the libraries was screened by PCR amplification with the PCR primer pair identified above. A positive library was then used to isolate clones encoding the PRO189 gene using the probe oligonucleotide and one of the PCR primers.

RNA for construction of the cDNA libraries was isolated from human retina tissue (LIB94). The cDNA libraries used to isolate the cDNA clones were constructed by standard methods using commercially available reagents such as those from Invitrogen, San Diego, CA. The cDNA was primed with oligo dT containing a NotI site, linked with blunt to SalI hemikinased adaptors, cleaved with NotI, sized appropriately by gel electrophoresis, and cloned in a defined orientation into a suitable cloning vector (such as pRKB or pRKD; pRK5B is a precursor of pRK5D that does not contain the SfiI site; see, Holmes et al., *Science*, 253:1278-1280 (1991)) in the unique XhoI and NotI sites.

DNA sequencing of the clones isolated as described above gave the full-length DNA sequence for PRO189 and the derived protein sequence for PRO189.

The entire nucleotide sequence of DNA21624-1391 is shown in Figure 5 (SEQ ID NO:7). Clone DNA21624-1391 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 200-202 and ending at the stop codon at nucleotide positions 1301-1303 (Figure 5). The predicted polypeptide precursor is 367 amino acids long (Figure 6). The full-length PRO189 protein shown in Figure 6 has an estimated molecular weight of about 41,871 daltons and a pI of about 5.06. Clone DNA21624-1391 has been deposited with the ATCC. Regarding the sequence, it is understood that the deposited clone contains the correct sequence, and the sequences provided herein are based on known sequencing techniques.

Analyzing the amino acid sequence of SEQ ID NO:8, the putative N-glycosylation sites are at about amino acids 224-227, 246-249 and 285-288. A domain for cytosolic fatty-acid binding proteins is at amino acids 78-107 of SEQ ID NO:8. The corresponding nucleotides can be routinely determined given the sequences provided herein.

Some sequence identity was found to W01A6.1 and F35D11.11, C. Elegans proteins, designated in a Dayhoff database as CEW01A6\_10 and CELF35D11\_11, respectively. Some sequence identity was also found to an antigen to malaria and to restin, designated in a Dayhoff database as P\_R05766 and AF014012\_1, respectively. Some sequence identity was also found to a microtubule binding protein and to myosin, designated in a Dayhoff database as AF041382\_1 and S07537, respectively. There is also some sequence identity with 1-phosphatidylinositol-4, 5-bisphosphate, designated as PIP1\_RAT.

EXAMPLE 7: Isolation of cDNA clones Encoding Human PRO190

A clone designated herein as DNA14232 was isolated as described in Example 2 above from a human fetal retina tissue library. The DNA14232 sequence is shown in Figure 10 (SEQ ID NO:15). Based on the DNA14232 sequence, oligonucleotides were synthesized: 1) to identify by PCR a cDNA library that contained

the sequence of interest, and 2) for use as probes to isolate a clone of the full-length coding sequence for PRO190. Forward and reverse PCR primers generally range from 20 to 30 nucleotides and are often designed to give a PCR product of about 100-1000 bp in length. The probe sequences are typically 40-55 bp in length. In order to screen several libraries for a full-length clone, DNA from the libraries was screened by PCR amplification, as per Ausubel et al., Current Protocols in Molecular Biology, with the PCR primer pair. A  
 5 positive library was then used to isolate clones encoding the gene of interest using the probe oligonucleotide and one of the primer pairs.

A pair of PCR primers (forward and reverse) were synthesized:

forward PCR primer 5'-CTATACCTACTGTAGCTTCT-3' (SEQ ID NO:16); and

reverse PCR primer 5'-TCAGAGAATTCCTTCCAGGA-3' (SEQ ID NO:17).

10 Additionally, a synthetic oligonucleotide hybridization probe was constructed from the DNA14232 sequence which had the following nucleotide sequence:

hybridization probe

5'-ACAGTGCTGTAGTCATCCTGTAATATGCTCCTTGCAACA-3' (SEQ ID NO:18).

In order to screen several libraries for a source of a full-length clone, DNA from the libraries was  
 15 screened by PCR amplification with the PCR primer pair identified above. A positive library was then used to isolate clones encoding the PRO190 gene using the probe oligonucleotide and one of the PCR primers.

RNA for construction of the cDNA libraries was isolated from human retina tissue (LIB94). The cDNA libraries used to isolate the cDNA clones were constructed by standard methods using commercially available reagents such as those from Invitrogen, San Diego, CA. The cDNA was primed with oligo dT containing a NotI site, linked with blunt to SalI hemikinased adaptors, cleaved with NotI, sized appropriately by gel  
 20 electrophoresis, and cloned in a defined orientation into a suitable cloning vector (such as pRKB or pRKD; pRK5B is a precursor of pRK5D that does not contain the SfiI site; see, Holmes et al., Science, 253:1278-1280 (1991)) in the unique XhoI and NotI sites.

DNA sequencing of the clones isolated as described above gave sequences which include the full-length  
 25 DNA sequence for PRO190 [herein designated as DNA23334-1392] (SEQ ID NO:13) and the derived protein sequence for PRO190.

The entire nucleotide sequence of DNA23334-1392 is shown in Figure 8 (SEQ ID NO:13). Clone DNA23334-1392 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 193-195 and which ends at the stop codon at nucleotide positions 1465-1467 (Figure 8). The predicted  
 30 polypeptide precursor is 424 amino acids long (Figure 9). The full-length PRO190 protein shown in Figure 9 has an estimated molecular weight of about 48,500 daltons and a pI of about 8.65. Clone DNA23334-1392 has been deposited with the ATCC. Regarding the sequence, it is understood that the deposited clone contains the correct sequence, and the sequences provided herein are based on known sequencing techniques.

Analyzing the amino acid sequence of SEQ ID NO:14, the putative transmembrane domains are at about  
 35 amino acids 16-36, 50-74, 147-168, 229-250, 271-293, 298-318 and 328-368 of SEQ ID NO:14. N-glycosylation sites are at about amino acids 128-131, 204-207, 218-221 and 274-377 of SEQ ID NO:14. The corresponding nucleotides can be routinely determined given the sequences provided herein.

PRO190 has sequence identity with at least the following Dayhoff sequences designated as: CEZK896\_2, JC5023, GMS1\_SCHPO and S44668.

**EXAMPLE 8: Isolation of cDNA clones Encoding Human PRO341**

A clone designated herein as DNA12920 was isolated as described in Example 2 above from a human placenta tissue library. The DNA12920 sequence is shown in Figure 13 (SEQ ID NO:21). The DNA12920 sequence was then compared to various EST databases including public EST databases (e.g., GenBank), and a proprietary EST database (LIFESEQ®, Incyte Pharmaceuticals, Palo Alto, CA) to identify homologous EST sequences. The comparison was performed using the computer program BLAST or BLAST2 [Altschul et al., *Methods in Enzymology*, 266:460-480 (1996)]. Those comparisons resulting in a BLAST score of 70 (or in some cases, 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). This consensus sequence is herein designated DNA25314. Oligonucleotide primers based upon the DNA25314 sequence were then synthesized and employed to screen a human placenta cDNA library which resulted in the identification of the DNA26288-1239 clone shown in Figure 11. The cloning vector was pRK5B (pRK5B is a precursor of pRK5D that does not contain the SfiI site; see, Holmes et al., *Science*, 253:1278-1280 (1991)), and the cDNA size cut was less than 2800 bp.

A full length clone was identified that contained a single open reading frame with an apparent translational initiation site at nucleotide positions 380-382, and a stop signal at nucleotide positions 1754-1756 (Figure 11, SEQ ID NO:19). The predicted polypeptide precursor is 458 amino acids long, has a calculated molecular weight of approximately 50,264 daltons and an estimated pI of approximately 8.17. Analysis of the full-length PRO341 sequence shown in Figure 12 (SEQ ID NO:20) evidences the presence of the following: a signal peptide from about amino acid 1 to about amino acid 17, transmembrane domains from about amino acid 171 to about amino acid 190, from about amino acid 220 to about amino acid 239, from about amino acid 259 to about amino acid 275, from about amino acid 286 to about amino acid 305, from about amino acid 316 to about amino acid 335, from about amino acid 353 to about amino acid 378 and from about amino acid 396 to about amino acid 417 and potential N-glycosylation sites from about amino acid 145 to about amino acid 147 and from about amino acid 155 to about amino acid 158. Clone DNA26288-1239 has been deposited with ATCC on April 21, 1998 and is assigned ATCC deposit no. 209792.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST-2 sequence alignment analysis of the full-length sequence shown in Figure 12 (SEQ ID NO:20), evidenced homology between the PRO341 amino acid sequence and the following Dayhoff sequences: S75696, H69788, D69852, A69888, B64918, F64752, LPU89276\_1, G64962, S52977 and S44253.

**EXAMPLE 9: Isolation of cDNA clones Encoding Human PRO180**

A clone designated herein as DNA12922 was isolated as described in Example 2 above from a human placenta tissue library. The DNA12922 sequence is shown in Figure 16 (SEQ ID NO:24). The DNA12922 sequence was then compared to various EST databases including public EST databases (e.g., GenBank), and a

proprietary EST database (LIFESEQ®, Incyte Pharmaceuticals, Palo Alto, CA) to identify homologous EST sequences. The comparison was performed using the computer program BLAST or BLAST2 [Altschul et al., *Methods in Enzymology*, 266:460-480 (1996)]. Those comparisons resulting in a BLAST score of 70 (or in some cases, 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington).

5 An oligonucleotide probe was formed based upon the consensus sequence obtained above. This probe had the following sequence.

5'-ACCTGTTAGAAATGTGGTGGTTTCAGCAAGGCCTCAGTTT (SEQ ID NO:25).

This probe was used to screen a human placenta library prepared as described in paragraph 1 of Example 2 above. The cloning vector was pRK5B (pRK5B is a precursor of pRK5D that does not contain the SfiI site; see, 10 Holmes et al., *Science*, 253:1278-1280 (1991)), and the cDNA size cut was less than 2800 bp. A clone designated herein as DNA26843-1389 was obtained.

The entire nucleotide sequence of DNA26843-1389 is shown in Figure 14 (SEQ ID NO:22). Clone DNA26843-1389 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 121-123 and ending at the stop codon at nucleotide positions 919-921 (Figure 14). The predicted 15 polypeptide precursor is 266 amino acids long (Figure 15). The full-length PRO180 protein shown in Figure 15 has an estimated molecular weight of about 29,766 daltons and a pI of about 8.39. Clone DNA26843-1389 has been deposited with the ATCC. Regarding the sequence, it is understood that the deposited clone contains the correct sequence, and the sequences provided herein are based on known sequencing techniques.

20 Still analyzing the amino acid sequence of SEQ ID NO:23, the transmembrane domains are at about amino acids 13-33 (type II), 54-73, 94-113, 160-180 and 122-141 of SEQ ID NO:23. N-myristoylation sites are at about amino acids 57-62, 95-100, 99-104, 124-129 and 183-188 of SEQ ID NO:23. The corresponding nucleotides can be routinely determined given the sequences provided herein.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 15 (SEQ ID NO:23), evidenced some sequence 25 identity between the PRO180 amino acid sequence and the following Dayhoff sequences: CEC33A11\_2, CEG11E6\_5, CELW03A5\_1 AND PEU83861\_2 (NADH dehydrogenase subunit 4L, mitochondrion).

#### EXAMPLE 10: Isolation of cDNA clones Encoding Human PRO194

30 A consensus DNA sequence was assembled relative to other EST sequences using phrap as described in Example 1 above. This consensus sequence is herein DNA19464. Based on the DNA19464 consensus sequence, oligonucleotides were synthesized: 1) to identify by PCR a cDNA library that contained the sequence of interest, and 2) for use as probes to isolate a clone of the full-length coding sequence for PRO194. PCR primers (forward and reverse) were synthesized based upon the DNA19464 sequence. Additionally, a synthetic oligonucleotide hybridization probe was constructed from the consensus DNA19464 sequence.

35 In order to screen several libraries for a source of a full-length clone, DNA from the libraries was screened by PCR amplification with the PCR primer pair identified above. A positive library was then used to isolate clones encoding the PRO194 gene using the probe oligonucleotide and one of the PCR primers. RNA

for construction of the cDNA libraries was isolated from human fetal lung tissue (LIB25).

DNA sequencing of the clones isolated as described above gave the full-length DNA sequence for PRO194 [herein designated as DNA26844-1394] (SEQ ID NO:27) and the derived protein sequence for PRO194.

The entire nucleotide sequence of DNA26844-1394 is shown in Figure 17 (SEQ ID NO:27). Clone  
 5 DNA26844-1394 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 81-83 and ending at the stop codon at nucleotide positions 873-875 (Figure 17). The predicted polypeptide precursor is 264 amino acids long (Figure 18). The full-length PRO194 protein shown in Figure 18 has an estimated molecular weight of about 29,665 daltons and a pI of about 9.34. Analysis of the full-length PRO194 sequence shown in Figure 18 (SEQ ID NO:28) evidences the presence of various important  
 10 polypeptides domains as shown in Figure 18. Clone DNA26844-1394 has been deposited with ATCC on June 2, 1998 and is assigned ATCC deposit no. 209926.

Analysis of the amino acid sequence of the full-length PRO194 polypeptide suggests that it does not exhibit significant sequence similarity to any known human protein. However, an analysis of the Dayhoff database (version 35.45 SwissProt 35) evidenced some homology between the PRO194 amino acid sequence and  
 15 the following Dayhoff sequences, HUMORFT\_1, CET07F10\_5, ATFCA9\_12, F64934, YDIX\_ECOLI, ATAF00065719F29G20.19, H70002, S76980, H64934 and S76385.

#### EXAMPLE 11: Isolation of cDNA clones Encoding Human PRO203

A clone designated herein as DNA15618 was isolated as described in Example 2 above from a human  
 20 fetal lung tissue library. The DNA15618 sequence is shown in Figure 21 (SEQ ID NO:31). Oligonucleotide probes were generated from the sequence of the DNA15618 molecule and were used to screen a human fetal lung library (LIB26) prepared as described in paragraph 1 of Example 2 above. The cloning vector was pRK5B (pRK5B is a precursor of pRK5D that does not contain the SfiI site; see, Holmes et al., *Science*, 253:1278-1280 (1991)), and the cDNA size cut was less than 2800 bp.

A full length clone was identified that contained a single open reading frame with an apparent  
 25 translational initiation site at nucleotide positions 159-161 and ending at the stop codon found at nucleotide positions 1200-1202 (Figure 19; SEQ ID NO:29). The predicted polypeptide precursor is 347 amino acids long, has a calculated molecular weight of approximately 39,870 daltons and an estimated pI of approximately 6.76. Analysis of the full-length PRO203 sequence shown in Figure 20 (SEQ ID NO:30) evidences the presence of  
 30 the following: a type II transmembrane domain at about amino acid 64 to about amino acid 87; possible N-glycosylation sites at about amino acid 147 to about amino acid 150, about amino acid 155 to about amino acid 158, and about amino acid 237 to about amino acid 240; sequence identity with heavy-metal-associated domain proteins at about amino acid 23 to about amino acid 45, and sequence identity with D-isomer specific 2-hydroxyacid dehydrogenase at about amino acid 24 to about amino acid 34. Clone DNA30862-1396 was  
 35 deposited with the ATCC on June 2, 1998, and is assigned ATCC deposit no. 209920.

Analysis of the amino acid sequence of the full-length PRO203 polypeptide suggests that it possesses sequence similarity to GST ATPase, thereby indicating that PRO203 may be a novel GST ATPase. More

specifically, an analysis of the Dayhoff database (version 35.45 SwissProt 35) evidenced homology between the PRO203 amino acid sequence and the following Dayhoff sequences, AF008124\_1, CFRCD1GEN\_1, and P\_R82566.

**EXAMPLE 12: Isolation of cDNA clones Encoding Human PRO290**

- 5 An expressed sequence tag (EST) DNA database (LIFESEQ®, Incyte Pharmaceuticals, Palo Alto, CA) was searched and an EST was identified that had homology to beige and FAN. An oligonucleotide probe based upon the identified EST sequence was then synthesized and used to screen human fetal kidney cDNA libraries in an attempt to identify a full-length cDNA clone. The oligonucleotide probe had the following sequence:  
 5' TGACTGCACTACCCCGTGGCAAGCTGTTGAGCCAGCTCAGCTG 3' (SEQ ID NO:34).
- 10 RNA for construction of cDNA libraries was isolated from human fetal kidney tissue. The cDNA libraries used to isolate the cDNA clones encoding human PRO290 were constructed by standard methods using commercially available reagents such as those from Invitrogen, San Diego, CA. The cDNA was primed with oligo dT containing a NotI site, linked with blunt to SalI hemikinased adaptors, cleaved with NotI, sized appropriately by gel electrophoresis, and cloned in a defined orientation into a suitable cloning vector (such as
- 15 pRKB or pRKD; pRK5B is a precursor of pRK5D that does not contain the SfiI site; see, Holmes et al., *Science* 253:1278-1280 (1991)) in the unique XhoI and NotI.

- A cDNA clone was identified and sequenced in entirety. The entire nucleotide sequence of DNA35680-1212 is shown in Figure 22 (SEQ ID NO:32). Clone DNA35680-1212 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 293-295, and a stop codon at nucleotide positions
- 20 3302-3304 (Figure 22; SEQ ID NO:32). The predicted polypeptide precursor is 1003 amino acids long.

- It is currently believed that the PRO290 polypeptide is related to FAN and/or beige. Clone DNA35680-1212 has been deposited with ATCC and is assigned ATCC deposit no. 209790. It is understood that the deposited clone has the actual correct sequence rather than the representations provided herein. The full-length PRO290 protein shown in Figure 23 has an estimated molecular weight of about 112,013 daltons and a pI of
- 25 about 6.4.

**EXAMPLE 13: Isolation of cDNA Clones Encoding Human PRO874**

- A consensus DNA sequence designated herein as DNA36459 was identified using phrap as described in Example 1 above. Based on the DNA36459 consensus sequence, oligonucleotides were synthesized: 1) to
- 30 identify by PCR a cDNA library that contained the sequence of interest, and 2) for use as probes to isolate a clone of the coding sequence for PRO874.

PCR primers (forward and reverse) were synthesized:

forward PCR primer 5'-TCGTGCCCAGGGGCTGATGTGC-3' (SEQ ID NO:37); and

reverse PCR primer 5'-GTCTTTACCCAGCCCCGGGATGCG-3' (SEQ ID NO:38).

- 35 Additionally, a synthetic oligonucleotide hybridization probe was constructed from the consensus DNA36459 sequence which had the following nucleotide sequence:

hybridization probe

5'-GGCCTAATCCAACGTTCTGTCTTCAATCTGCAAATCTATGGGGTCCTGGG-3' (SEQ ID NO:39).

In order to screen several libraries for a source of a clone, DNA from the libraries was screened by PCR amplification with the PCR primer pair identified above. A positive library was then used to isolate clones encoding the PRO874 gene using the probe oligonucleotide and one of the PCR primers. RNA for construction of the cDNA libraries was isolated from human fetal lung tissue (LIB25).

DNA sequencing of the clones isolated as described above gave the DNA sequence for PRO874 [herein designated as DNA40621-1440] (SEQ ID NO:35) and the derived protein sequence for PRO874.

The entire nucleotide sequence of DNA40621-1440 is shown in Figure 24 (SEQ ID NO:35). Clone DNA40621-1440 contains a single open reading frame ending at the stop codon at nucleotide positions 964-966 (Figure 24). The predicted polypeptide encoded by DNA40621-1440 is 321 amino acids long (Figure 25). The PRO874 protein shown in Figure 25 has an estimated molecular weight of about 36,194 daltons and a pI of about 9.85. Analysis of the PRO874 sequence shown in Figure 25 (SEQ ID NO:36) evidenced the presence of the following: a type II transmembrane domain at about amino acids 57-80; additional transmembrane domains at about amino acids 110-126, 215-231, and 254-274; potential N-glycosylation sites at about amino acids 16-19, 27-30, and 289-292; sequence identity with hypothetical YBR002c family proteins at about amino acids 276-287; and sequence identity with ammonium transporter proteins at about amino acids 204-230. Clone DNA40621-1440 was deposited with the ATCC on June 2, 1998, and is assigned ATCC deposit no. 209922.

Analysis of the amino acid sequence of the PRO874 polypeptide suggests that it is a novel multi-span transmembrane protein. However, an analysis of the Dayhoff database (version 35.45 SwissProt 35) evidenced sequence identity between the PRO874 amino acid sequence and the following Dayhoff sequences: S67049, AF054839\_1, S73437, S52460, and HIVU80570\_1.

EXAMPLE 14: Isolation of cDNA Clones Encoding Human PRO710

A yeast screening assay was employed to identify cDNA clones that encoded potential secreted proteins. Use of this yeast screening assay allowed identification of a single cDNA clone whose sequence (herein designated as DNA38190) is shown in Figure 28 (SEQ ID NO:42). Based on the DNA38190 sequence shown in Figure 28, oligonucleotides were synthesized: 1) to identify by PCR a cDNA library that contained the sequence of interest, and 2) for use as probes to isolate a clone of the full-length coding sequence for PRO710. In order to screen several libraries for a full-length clone, DNA from the libraries was screened by PCR amplification, as per Ausubel et al., Current Protocols in Molecular Biology, with the PCR primer pair. A positive library was then used to isolate clones encoding the gene of interest using the probe oligonucleotide and one of the primer pairs.

PCR primers (forward and reverse) were synthesized:

forward PCR primer 5'-TTCCGCAAAGAGTTCTACGAGGTGG-3' (SEQ ID NO:43)

reverse PCR primer 5'-ATTGACAACATTGACTGGCCTATGGG-3' (SEQ ID NO:44)

Additionally, a synthetic oligonucleotide hybridization probe was constructed from the DNA38190 sequence which had the following nucleotide sequence

hybridization probe

5'-GTGGATGCTCTGTGTGCGTGCAAGATCCTTCAGGCCTTGTTCCAGTGTGA-3' (SEQ ID NO:45)

In order to screen several libraries for a source of a full-length clone, DNA from the libraries was screened by PCR amplification with the PCR primer pair identified above. A positive library was then used to isolate clones encoding the PRO710 gene using the probe oligonucleotide and one of the PCR primers.

- 5 RNA for construction of the cDNA libraries was isolated from human fetal kidney tissue (LIB227). The cDNA libraries used to isolate the cDNA clones were constructed by standard methods using commercially available reagents such as those from Invitrogen, San Diego, CA. The cDNA was primed with oligo dT containing a NotI site, linked with blunt to SalI hemikinased adaptors, cleaved with NotI, sized appropriately by gel electrophoresis, and cloned in a defined orientation into a suitable cloning vector (such as pRKB or pRKD; pRK5B is a precursor of pRK5D that does not contain the SfiI site; see, Holmes et al., Science, 253:1278-1280 (1991)) in the unique XhoI and NotI sites.

- 15 A full length clone was identified that contained a single open reading frame with an apparent translational initiation site at nucleotide positions 67-69 and ending at the stop codon found at nucleotide positions 1765-1767 (Figure 26, SEQ ID NO:40). The predicted polypeptide precursor is 566 amino acids long, has a calculated molecular weight of approximately 65,555 daltons and an estimated pI of approximately 5.44. Analysis of the full-length PRO710 sequence shown in Figure 27 (SEQ ID NO:41) evidences the presence of the following: a signal peptide from about amino acid 1 to about amino acid 32, a transmembrane domain from about amino acid 454 to about amino acid 476, an aminoacyl-transfer RNA synthetase class-II signature sequence from about amino acid 6 to about amino acid 26 and potential N-glycosylation sites from about amino acid 111 to about amino acid 114, from about amino acid 146 to about amino acid 149 and from about amino acid 292 to about amino acid 295. Clone DNA44161-1434 has been deposited with ATCC on May 27, 1998 and is assigned ATCC deposit no. 209907.

- 25 Analysis of the amino acid sequence of the full-length PRO710 polypeptide suggests that it possesses significant sequence similarity to the CDC45 protein, thereby indicating that PRO710 may be a novel CDC45 homolog. More specifically, an analysis of the Dayhoff database (version 35.45 SwissProt 35) evidenced significant homology between the PRO710 amino acid sequence and the following Dayhoff sequences, HSAJ3728\_1, CEF34D10\_1, S64939, UMUS0276\_1, TRHY\_SHEEP, CELT14E8\_1, RNA1\_YEAST, LVU89340\_1, HSU80736\_1 and CEZK337\_2.

30 EXAMPLE 15: Isolation of cDNA clones Encoding Human PRO1151

- A consensus DNA sequence was assembled relative to other EST sequences using phrap as described in Example 1 above. This consensus sequence is herein designated DNA40665. Based on the DNA40665 consensus sequence, oligonucleotides were synthesized: 1) to identify by PCR a cDNA library that contained the sequence of interest, and 2) for use as probes to isolate a clone of the full-length coding sequence for PRO1151.
- 35



PCR primers (forward and reverse) were synthesized:

forward PCR primer 5'-CCAGACGCTGCTCTTCGAAAGGGTC-3' (SEQ ID NO:48)

reverse PCR primer 5'-GGTCCCCGTAGGCCAGGTCCAGC-3' (SEQ ID NO:49)

Additionally, a synthetic oligonucleotide hybridization probe was constructed from the consensus DNA40665 sequence which had the following nucleotide sequence

5 hybridization probe

5'-CTACTTCTTCAGCCTCAATGTGCACAGCTGGAATTACAAGGAGACGTACG-3' (SEQ ID NO:50)

In order to screen several libraries for a source of a full-length clone, DNA from the libraries was screened by PCR amplification with the PCR primer pair identified above. A positive library was then used to isolate clones encoding the PRO1151 gene using the probe oligonucleotide and one of the PCR primers. RNA  
10 for construction of the cDNA libraries was isolated from human fetal kidney tissue.

DNA sequencing of the clones isolated as described above gave the full-length DNA sequence for PRO1151 (designated herein as DNA44694-1500 [Figure 29, SEQ ID NO:46]; and the derived protein sequence for PRO1151.

The entire nucleotide sequence of DNA44694-1500 is shown in Figure 29 (SEQ ID NO:46). Clone  
15 DNA44694-1500 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 272-274 and ending at the stop codon at nucleotide positions 1049-1051 (Figure 29). The predicted polypeptide precursor is 259 amino acids long (Figure 30). The full-length PRO1151 protein shown in Figure 30 has an estimated molecular weight of about 28,770 daltons and a pI of about 6.12. Analysis of the full-length PRO1151 sequence shown in Figure 30 (SEQ ID NO:47) evidences the presence of the following: a signal  
20 peptide from about amino acid 1 to about amino acid 20, a potential N-glycosylation site from about amino acid 72 to about amino acid 75 and amino acid sequence blocks having homology to C1q domain-containing proteins from about amino acid 144 to about amino acid 178, from about amino acid 78 to about amino acid 111 and from about amino acid 84 to about amino acid 117. Clone UNQ581 (DNA44694-1500) has been deposited with ATCC on August 11, 1998 and is assigned ATCC deposit no. 203114.

25 An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST-2 sequence alignment analysis of the full-length sequence shown in Figure 30 (SEQ ID NO:47), evidenced significant homology between the PRO1151 amino acid sequence and the following Dayhoff sequences: ACR3\_HUMAN, HP25\_TAMAS, HUMC1QB2\_1, P\_R99306, CA1F\_HUMAN, JX0369, CA24\_HUMAN, S32436, P\_R28916 and CA54\_HUMAN.

30

EXAMPLE 16: Isolation of cDNA clones Encoding Human PRO1282

A consensus DNA sequence was assembled relative to other EST sequences using phrap as described in Example 1 above. This consensus sequence is designated herein as DNA33778. Based on the DNA33778 consensus sequence, oligonucleotides were synthesized: 1) to identify by PCR a cDNA library that contained  
35 the sequence of interest, and 2) for use as probes to isolate a clone of the full-length coding sequence for PRO1282.

PCR primers (forward and reverse) were synthesized:

forward PCR primer 5'TCTTCAGCCGCTTGCGCAACCTC3' (SEQ ID NO:53); and  
reverse PCR primer 5'TTGCTCACATCCAGCTCCTGCAGG3' (SEQ ID NO:54).

Additionally, a synthetic oligonucleotide hybridization probe was constructed from the consensus DNA33778 sequence which had the following nucleotide sequence:

5 hybridization probe

5'TGGATGTTGTCCAGACAACCAGCTGGAGCTGTATCCGAGGC3' (SEQ ID NO:55).

In order to screen several libraries for a source of a full-length clone, DNA from the libraries was screened by PCR amplification with the PCR primer pair identified above. A positive library was then used to isolate clones encoding the PRO1282 gene using the probe oligonucleotide and one of the PCR primers. RNA  
10 for construction of the cDNA libraries was isolated from human fetal liver.

DNA sequencing of the clones isolated as described above gave the full-length DNA sequence for PRO1282 (designated herein as DNA45495-1550 [Figure 31, SEQ ID NO:51]; and the derived protein sequence for PRO1282.

The entire coding sequence of PRO1282 is shown in Figure 31 (SEQ ID NO:51). Clone DNA45495-  
15 1550 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 120-122, and an apparent stop codon at nucleotide positions 2139-2141 (SEQ ID NO:51). The predicted polypeptide precursor is 673 amino acids long. The signal peptide is at about amino acids 1-23; the transmembrane domain is at about amino acids 579-599; an EGF-like domain cysteine pattern signature starts at about amino acid 430; and leucine zipper patterns start at about amino acids 197 and 269 of SEQ ID NO:52,  
20 see Figure 32. Clone DNA45495-1550 has been deposited with the ATCC and is assigned ATCC deposit no. 203156. The full-length PRO1282 protein shown in Figure 32 has an estimated molecular weight of about 71,655 daltons and a pI of about 7.8.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST-2 sequence alignment analysis of the full-length sequence shown in Figure 32 (SEQ ID NO:52), revealed sequence identity  
25 between the PRO1282 amino acid sequence and the following Dayhoff sequences (data from database incorporated by reference): AB007876\_1, RNPLGPV\_1, MUSLRRP\_1, ALS\_PAPPA, AC004142\_1, ALS\_HUMAN, AB014462\_1, DMTARTAN\_1, HSCHON03\_1 and S46224.

EXAMPLE 17: Isolation of cDNA clones Encoding Human PRO358

30 Using the method described in Example 1 above, a single EST sequence was identified in the Incyte database, designated herein as INC3115949. Based on the INC3115949 EST sequence, oligonucleotides were synthesized to identify by PCR a cDNA library that contained the sequence of interest and for use as probes to isolate a clone of the full-length coding sequence for PRO358.

A pair of PCR primers (forward and reverse) were synthesized:

35 forward PCR primer 5'-TCCCACCAGGTATCATAAACTGAA-3' (SEQ ID NO:58)  
reverse PCR primer 5'-TTATAGACAATCTGTTCTCATCAGAGA-3' (SEQ ID NO:59)

A probe was also synthesized:

5'-AAAAAGCATACTTGGGAATGGCCCAAGGATAGGTGTAATG-3' (SEQ ID NO:60)

In order to screen several libraries for a source of a full-length clone, DNA from the libraries was screened by PCR amplification with the PCR primer pair identified above. A positive library was then used to isolate clones encoding the PRO358 gene using the probe oligonucleotide and one of the PCR primers. RNA  
5 for construction of the cDNA libraries was isolated from human bone marrow (LIB256). The cDNA libraries used to isolated the cDNA clones were constructed by standard methods using commercially available reagents such as those from Invitrogen, San Diego, CA. The cDNA was primed with oligo dT containing a NotI site, linked with blunt to SalI hemikinased adaptors, cleaved with NotI, sized appropriately by gel electrophoresis, and cloned in a defined orientation into a suitable cloning vector (such as pRKB or pRKD; pRK5B is a precursor  
10 of pRK5D that does not contain the SfiI site; see, Holmes et al., *Science*, 253:1278-1280 (1991)) in the unique XhoI and NotI sites.

DNA sequencing of the clones isolated as described above gave the full-length DNA sequence for PRO358 (Figure 33, SEQ ID NO:56) and the derived protein sequence for PRO358 (Figures 34, SEQ ID NO:57).

15 The entire nucleotide sequence of the clone identified (DNA47361-1154) is shown in Figure 33 (SEQ ID NO:56). Clone DNA47361-1154 contains a single open reading frame with an apparent translational initiation site (ATG start signal) at nucleotide positions underlined in Figure 33. The predicted polypeptide precursor is 811 amino acids long, including a putative signal sequence (amino acids 1 to 19), an extracellular domain (amino acids 20 to 575, including leucine rich repeats in the region from position 55 to position 575),  
20 a putative transmembrane domain (amino acids 576 to 595). Clone DNA47361-1249 has been deposited with ATCC and is assigned ATCC deposit no. 209431.

#### EXAMPLE 18: Isolation of cDNA clones Encoding Human PRO1310

A consensus DNA sequence was assembled relative to other EST sequences using phrap as described  
25 in Example 1 above. This consensus sequence is designated herein as DNA37164. Based on the DNA37164 consensus sequence, oligonucleotides were synthesized: 1) to identify by PCR a cDNA library that contained the sequence of interest, and 2) for use as probes to isolate a clone of the full-length coding sequence for PRO1310.

PCR primers (forward and reverse) were synthesized:

30 forward PCR primer: 5'GTTCTCAATGAGCTACCCGTCCCC3' (SEQ ID NO:63) and  
reverse PCR primer: 5'CGCGATGTAGTGGAACCTCGGGCTC3' (SEQ ID NO:64).

Additionally, a synthetic oligonucleotide hybridization probe was constructed from the consensus DNA47394 sequence which had the following nucleotide sequence:

hybridization probe:

35 5'ATCCGCATAAACCCCTCAGTCCTGGTTTGATAATGGGAGCATCTGCATGAG3' (SEQ ID NO:65).

In order to screen several libraries for a source of a full-length clone, DNA from the libraries was screened by PCR amplification with the PCR primer pair identified above. A positive library was then used to

isolate clones encoding the PRO1310 gene using the probe oligonucleotide and one of the PCR primers. RNA for construction of the cDNA libraries was isolated from human fetal liver tissue.

DNA sequencing of the clones isolated as described above gave the full-length DNA sequence for PRO1310 and the derived protein sequence for PRO1310.

The entire coding sequence of PRO1310 is shown in Figures 35A-B (SEQ ID NO:61). Clone  
 5 DNA47394-1572 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 326-328, and an apparent stop codon at nucleotide positions 2594-2596 (SEQ ID NO:61). The predicted polypeptide precursor is 765 amino acids long. The signal peptide is at about amino acids 1-25 of SEQ ID NO:62. Clone DNA47394-1572 has been deposited with ATCC and is assigned ATCC deposit no. 203109. The full-length PRO1310 protein shown in Figure 36 has an estimated molecular weight of about 85,898 daltons  
 10 and a pI of about 6.87.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST-2 sequence alignment analysis of the full-length sequence shown in Figure 36 (SEQ ID NO:62), revealed sequence identity between the PRO1310 amino acid sequence and the following Dayhoff sequences: AF017639\_1, P\_W36817, JC5256, CBPH\_HUMAN, MMU23184\_1, CBPN\_HUMAN, HSU83411\_1, CEF01D4\_7, RNU62897\_1 and  
 15 P\_W11851.

#### EXAMPLE 19: Isolation of cDNA Clones Encoding Human PRO698

A yeast screening assay was employed to identify cDNA clones that encoded potential secreted proteins. Use of this yeast screening assay allowed identification of a single cDNA clone whose sequence (herein  
 20 designated as DNA39906) is shown in Figure 39 (SEQ ID NO:68). Based on the DNA39906 sequence shown in Figure 39, oligonucleotides were synthesized: 1) to identify by PCR a cDNA library that contained the sequence of interest, and 2) for use as probes to isolate a clone of the full-length coding sequence for PRO698. In order to screen several libraries for a full-length clone, DNA from the libraries was screened by PCR amplification, as per Ausubel et al., Current Protocols in Molecular Biology, with the PCR primer pair. A  
 25 positive library was then used to isolate clones encoding the gene of interest using the probe oligonucleotide and one of the primer pairs.

PCR primers (forward and reverse) were synthesized:

forward PCR primer 5'-AGCTGTGGTCATGGTGGTGTGGTG-3' (SEQ ID NO:69)

reverse PCR primer 5'-CTACCTTGGCCATAGGTGATCCGC-3' (SEQ ID NO:70)

30 Additionally, a synthetic oligonucleotide hybridization probe was constructed from the consensus DNA39906 sequence which had the following nucleotide sequence

hybridization probe

5'-CATCAGCAAACCGTCTGTGGTTCAGCTCAACTGGAGAGGGTT-3' (SEQ ID NO:71)

In order to screen several libraries for a source of a full-length clone, DNA from the libraries was  
 35 screened by PCR amplification with the PCR primer pair identified above. A positive library was then used to isolate clones encoding the PRO698 gene using the probe oligonucleotide and one of the PCR primers. RNA for construction of the cDNA libraries was isolated from human bone marrow tissue (LIB255). The cDNA

libraries used to isolate the cDNA clones were constructed by standard methods using commercially available reagents such as those from Invitrogen, San Diego, CA. The cDNA was primed with oligo dT containing a NotI site, linked with blunt to SalI hemikinased adaptors, cleaved with NotI, sized appropriately by gel electrophoresis, and cloned in a defined orientation into a suitable cloning vector (such as pRKB or pRKD; pRK5B is a precursor of pRK5D that does not contain the SfiI site; see, Holmes et al., *Science*, 253:1278-1280 (1991)) in the unique XhoI and NotI sites.

A full length clone was identified that contained a single open reading frame with an apparent translational initiation site at nucleotide positions 14-16 and ending at the stop codon found at nucleotide positions 1544-1546 (Figure 37, SEQ ID NO:66). The predicted polypeptide precursor is 510 amino acids long, has a calculated molecular weight of approximately 57,280 daltons and an estimated pI of approximately 5.61.

Analysis of the full-length PRO698 sequence shown in Figure 38 (SEQ ID NO:67) evidences the presence of the following: a signal peptide from about amino acid 1 to about amino acid 20, potential N-glycosylation sites from about amino acid 72 to about amino acid 75, from about amino acid 136 to about amino acid 139, from about amino acid 193 to about amino acid 196, from about amino acid 253 to about amino acid 256, from about amino acid 352 to about amino acid 355 and from about amino acid 411 to about amino acid 414 an amino acid block having homology to legume lectin beta-chain proteins from about amino acid 20 to about amino acid 39 and an amino acid block having homology to the HBGF/FGF family of proteins from about amino acid 338 to about amino acid 365. Clone DNA48320-1433 has been deposited with ATCC on May 27, 1998 and is assigned ATCC deposit no. 209904.

Analysis of the amino acid sequence of the full-length PRO698 polypeptide suggests that it possesses significant sequence similarity to the olfactomedin protein, thereby indicating that PRO698 may be a novel olfactomedin homolog. More specifically, an analysis of the Dayhoff database (version 35.45 SwissProt 35) evidenced significant homology between the PRO698 amino acid sequence and the following Dayhoff sequences, OLFM\_RANCA, I73637, AB006686S3\_1, RNU78105\_1, RNU72487\_1, P\_R98225, CELC48E7\_4, CEF11C3\_3, XLU85970\_1 and S42257.

#### EXAMPLE 20: Isolation of cDNA Clones Encoding Human PRO732

A yeast screening assay was employed to identify cDNA clones that encoded potential secreted proteins. Use of this yeast screening assay allowed identification of a single cDNA clone whose sequence (herein designated as DNA42580) is shown in Figure 45 (SEQ ID NO:77). The DNA42580 sequence was then compared to a variety of known EST sequences to identify homologies. The EST databases employed included public EST databases (e.g., GenBank) and a proprietary EST DNA database (LIFESEQ™, Incyte Pharmaceuticals, Palo Alto, CA). The search was performed using the computer program BLAST or BLAST2 (Altschul et al., *Methods in Enzymology* 266:460-480 (1996)) as a comparison to a 6 frame translation of the EST sequence. Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into consensus DNA sequences with the program "phrap" (Phil Green, University of Washington, Seattle, Washington).

Using the above analysis, a consensus DNA sequence was assembled relative to other EST sequences using phrap. This consensus sequence is herein designated consen01. Proprietary Genentech EST sequences were employed in the consensus assembly and they are herein designated DNA20239 (Figure 42; SEQ ID NO:74), DNA38050 (Figure 43; SEQ ID NO:75) and DNA40683 (Figure 44; SEQ ID NO:76).

Based on the consen01 sequence, oligonucleotides were synthesized: 1) to identify by PCR a cDNA library that contained the sequence of interest, and 2) for use as probes to isolate a clone of the full-length coding sequence for PRO732. Forward and reverse PCR primers generally range from 20 to 30 nucleotides and are often designed to give a PCR product of about 100-1000 bp in length. The probe sequences are typically 40-55 bp in length. In some cases, additional oligonucleotides are synthesized when the consensus sequence is greater than about 1-1.5kbp. In order to screen several libraries for a full-length clone, DNA from the libraries was screened by PCR amplification, as per Ausubel et al., Current Protocols in Molecular Biology, with the PCR primer pair. A positive library was then used to isolate clones encoding the gene of interest using the probe oligonucleotide and one of the primer pairs.

PCR primers (forward and reverse) were synthesized:

forward PCR primer 5'-ATGTTTGTGTGGAAGTGCCCG-3' (SEQ ID NO:78)

forward PCR primer 5'-GTCAACATGCTCCTCTGC-3' (SEQ ID NO:79)

reverse PCR primer 5'-AATCCATTGTGCACTGCAGCTCTAGG-3' (SEQ ID NO:80)

reverse PCR primer 5'-GAGCATGCCACCACTGGACTGAC-3' (SEQ ID NO:81)

Additionally, a synthetic oligonucleotide hybridization probe was constructed from the consensus DNA44143 sequence which had the following nucleotide sequence

hybridization probe

5'-GCCGATGCTGCTCCTAGTGGAACAACCTCCACTGTAAGTAGATTGATCTATGCAC-3' (SEQ ID NO:82)

In order to screen several libraries for a source of a full-length clone, DNA from the libraries was screened by PCR amplification with the PCR primer pairs identified above. A positive library was then used to isolate clones encoding the PRO732 gene using the probe oligonucleotide and one of the PCR primers.

RNA for construction of the cDNA libraries was isolated from human fetal lung tissue (LIB26). The cDNA libraries used to isolate the cDNA clones were constructed by standard methods using commercially available reagents such as those from Invitrogen, San Diego, CA. The cDNA was primed with oligo dT containing a NotI site, linked with blunt to SalI hemikinased adaptors, cleaved with NotI, sized appropriately by gel electrophoresis, and cloned in a defined orientation into a suitable cloning vector (such as pRKB or pRKD; pRK5B is a precursor of pRK5D that does not contain the SfiI site; see, Holmes et al., Science, 253:1278-1280 (1991)) in the unique XhoI and NotI sites.

A full length clone was identified that contained a single open reading frame with an apparent translational initiation site at nucleotide positions 88-90 and ending at the stop codon found at nucleotide positions 1447-1449 (Figure 40, SEQ ID NO:72). The predicted polypeptide precursor is 453 amino acids long, has a calculated molecular weight of approximately 50,419 daltons and an estimated pI of approximately 5.78. Analysis of the full-length PRO732 sequence shown in Figure 41 (SEQ ID NO:73) evidences the presence of

the following: a signal peptide from about amino acid 1 to about amino acid 28, transmembrane domains from about amino acid 37 to about amino acid 57, from about amino acid 93 to about amino acid 109, from about amino acid 126 to about amino acid 148, from about amino acid 151 to about amino acid 172, from about amino acid 197 to about amino acid 215, from about amino acid 231 to about amino acid 245, from about amino acid 260 to about amino acid 279, from about amino acid 315 to about amino acid 333, from about amino acid 384  
 5 to about amino acid 403 and from about amino acid 422 to about amino acid 447, potential N-glycosylation sites from about amino acid 33 to about amino acid 36, from about amino acid 34 to about amino acid 37, from about amino acid 179 to about amino acid 183, from about amino acid 298 to about amino acid 301, from about amino acid 337 to about amino acid 340 and from about amino acid 406 to about amino acid 409, an amino acid block having homology to the MIP family of proteins from about amino acid 119 to about amino acid 149 and an  
 10 amino acid block having homology to DNA/RNA non-specific endonuclease proteins from about amino acid 279 to about amino acid 286. Clone DNA48334-1435 has been deposited with ATCC on June 2, 1998 and is assigned ATCC deposit no. 209924.

Analysis of the amino acid sequence of the full-length PRO732 polypeptide suggests that it possesses significant sequence similarity to the Diff33 protein, thereby indicating that PRO732 may be a novel Diff33  
 15 homolog. More specifically, an analysis of the Dayhoff database (version 35.45 SwissProt 35) evidenced significant homology between the PRO732 amino acid sequence and the following Dayhoff sequences, HS179M20\_2, MUSTETU\_1, CER11H6\_2, RATDRP\_1, S51256, E69226, AE000869\_1, JC4120, CYB\_PARTE and P\_R50619.

## 20 EXAMPLE 21: Isolation of cDNA clones Encoding Human PRO1120

A consensus DNA sequence was assembled relative to other EST sequences using phrap as described in Example 1 above. This consensus sequence is designated herein consen0352. The consen0352 sequence was then extended using repeated cycles of BLAST and phrap to extend the consensus sequence as far as possible using the sources of EST sequences discussed above. The extended consensus sequence is designated herein as  
 25 DNA34365. Based on the DNA34365 consensus sequence, oligonucleotides were synthesized: 1) to identify by PCR a cDNA library that contained the sequence of interest, and 2) for use as probes to isolate a clone of the full-length coding sequence for PRO1120.

PCR primers (forward and reverse) were synthesized:

forward PCR primers: 5'-GAAGCCGGCTGTCTGAATC-3' (SEQ ID NO:85),  
 30 5'-GGCCAGCTATCTCCGAG-3' (SEQ ID NO:86), 5'-AAGGGCCTGCAAGAGAAG-3' (SEQ ID NO:87),  
 5'-CACTGGGACAACTGTGGG-3' (SEQ ID NO:88),  
 5'-CAGAGGCAACGTGGAGAG-3' (SEQ ID NO:89), and  
 5'-AAGTATTGTCATACAGTGTTC-3' (SEQ ID NO:90);  
reverse PCR primers: 5'-TAGTACTTGGGCACGAGTTGGAG-3' (SEQ ID NO:91), and 5'-  
 35 TCATACCAACTGCTGGTCATTGGC-3' (SEQ ID NO:92).

Additionally, a synthetic oligonucleotide hybridization probe was constructed from the DNA34365 consensus sequence which had the following nucleotide sequence:

hybridization probe:

5'-CTCAAGCTGCTGGACACGGAGCGGCCGGTGAATCGGTTTCACTTG-3' (SEQ ID NO:93).

In order to screen several libraries for a source of a full-length clone, DNA from the libraries was screened by PCR amplification with the PCR primer pairs identified above. A positive library was then used to isolate clones encoding the PRO1120 gene using the probe oligonucleotide and one of the PCR primers. RNA for construction of the cDNA libraries was isolated from human fetal kidney tissue.

DNA sequencing of the clones isolated as described above gave the full-length DNA sequence for PRO1120 (designated herein as DNA48606-1479 [Figures 46A-B, SEQ ID NO:83]; and the derived protein sequence for PRO1120.

The entire coding sequence of PRO1120 is shown in Figures 46A-B (SEQ ID NO:83). Clone DNA48606-1479 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 608-610 and an apparent stop codon at nucleotide positions 3209-3211. The predicted polypeptide precursor is 867 amino acids long. The full-length PRO1120 protein shown in Figure 47 has an estimated molecular weight of about 100,156 Daltons and a pI of about 9.44. Additional features of the PRO1120 polypeptide include a signal peptide at about amino acids 1-17; a sulfatase signature at about amino acids 86-98; regions of homology to sulfatases at about amino acids 87-106, 133-146, 216-229, 291-320, and 365-375; and potential N-glycosylation sites at about amino acids 65-68, 112-115, 132-135, 149-152, 171-174, 198-201, 241-245, 561-564, 608-611, 717-720, 754-757, and 764-767.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST-2 sequence alignment analysis of the full-length sequence shown in Figure 47 (SEQ ID NO:84), revealed significant homology between the PRO1120 amino acid sequence and the following Dayhoff sequences: CELK09C4\_1, GL6S\_HUMAN, G65169, NCU89492\_1, BCU44852\_1, E64903, P\_R51355, STS\_HUMAN, GA6S\_HUMAN, and IDS\_MOUSE. Clone DNA48606-1479 was deposited with the ATCC on July 1, 1998, and is assigned ATCC deposit no. 203040.

#### 25 EXAMPLE 22: Isolation of cDNA clones Encoding Human PRO537

Use of the signal sequence algorithm described in Example 3 above allowed identification of an EST cluster sequence from the Incyte database, designated as Incyte EST cluster no. 29605. This EST cluster sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (LIFESEQ®, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altschul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated DNA48350.

In light of an observed sequence homology between the DNA48350 consensus sequence and an EST sequence encompassed within the Merck EST clone no. R63443, the Merck EST clone R63443 was purchased and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein.



The sequence of this cDNA insert is shown in Figure 48 and is herein designated as DNA49141-1431.

Clone DNA49141-1431 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 97-99 and ending at the stop codon at nucleotide positions 442-444 (Figure 48). The predicted polypeptide precursor is 115 amino acids long (Figure 49). The full-length PRO537 protein shown in Figure 49 has an estimated molecular weight of about 13,183 daltons and a pI of about 12.13. Analysis of the full-length PRO537 sequence shown in Figure 49 (SEQ ID NO:95) evidences the presence of the following:

5 a signal peptide from about amino acid 1 to about amino acid 31, a potential N-glycosylation site from about amino acid 44 to about amino acid 47, potential N-myristylation sites from about amino acid 3 to about amino acid 8 and from about amino acid 16 to about amino acid 21 and an amino acid block having homology to multicopper oxidase proteins from about amino acid 97 to about amino acid 105. Clone DNA49141-1431 has

10 been deposited with ATCC on June 23, 1998 and is assigned ATCC deposit no. 203003.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST-2 sequence alignment analysis of the full-length sequence shown in Figure 49 (SEQ ID NO:95), evidenced homology between the PRO537 amino acid sequence and the following Dayhoff sequences: A54523, CELF22H10\_2, FK44\_MOUSE, OTX1\_HUMAN, URB1\_USTMA, KNOB\_PLAFN, A32895\_1, AF036332\_1, HRG\_HUMAN

15 and HRP3\_PLAFS.

#### EXAMPLE 23: Isolation of cDNA clones Encoding Human PRO536

Use of the signal sequence algorithm described in Example 3 above allowed identification of an EST cluster sequence from the Incyte database, designated herein as ss.clu2437.init. This EST cluster sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (LIFESEQ<sup>®</sup>, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altschul et al., *Methods in Enzymology* 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated DNA48351.

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In light of an observed sequence homology between the DNA48351 consensus sequence and an EST sequence encompassed within the Merck EST clone no. H11129, the Merck EST clone H11129 was purchased and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein.

30 The sequence of this cDNA insert is shown in Figure 50 and is herein designated as DNA49142-1430.

Clone DNA49142-1430 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 48-50 and ending at the stop codon at nucleotide positions 987-989 (Figure 50). The predicted polypeptide precursor is 313 amino acids long (Figure 51). The full-length PRO536 protein shown in Figure 51 has an estimated molecular weight of about 34,189 daltons and a pI of about 4.8. Analysis of the full-length PRO536 sequence shown in Figure 51 (SEQ ID NO:97) evidences the presence of the following: a signal peptide from about amino acid 1 to about amino acid 25, a potential N-glycosylation site from about amino acid 45 to about amino acid 48 and an amino acid sequence block having homology to sulfatase proteins from

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about amino acid 16 to about amino acid 26. Clone DNA49142-1430 has been deposited with ATCC on June 23, 1998 and is assigned ATCC deposit no. 203002.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST-2 sequence alignment analysis of the full-length sequence shown in Figure 51 (SEQ ID NO:97), evidenced homology between the PRO536 amino acid sequence and the following Dayhoff sequences: APU46857\_1, PK2\_DICDI,  
 5 H64743, F5I14\_18, CEAM\_ECOLI, GEN14267, H64965, TCU39815\_1, PSBJ\_ODOSI and P\_R06980.

#### EXAMPLE 24: Isolation of cDNA clones Encoding Human PRO535

Use of the signal sequence algorithm described in Example 3 above allowed identification of an EST cluster sequence from the Incyte database, designated herein as ss.clu12694.init. This EST cluster sequence was  
 10 then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (LIFESEQ®, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altschul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and  
 15 assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated DNA48352. Two proprietary Genentech EST sequences were employed in the assembly are herein shown in Figures 54 and 55.

In light of an observed sequence homology between the DNA48352 consensus sequence and an EST  
 20 sequence encompassed within the Merck EST clone no. H86994, the Merck EST clone H86994 was purchased and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein. The sequence of this cDNA insert is shown in Figure 52 and is herein designated as DNA49143-1429.

Clone DNA49143-1429 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 78-80 and ending at the stop codon at nucleotide positions 681-683 (Figure 52). The  
 25 predicted polypeptide precursor is 201 amino acids long (Figure 53). The full-length PRO535 protein shown in Figure 53 has an estimated molecular weight of about 22,180 daltons and a pI of about 9.68. Analysis of the full-length PRO535 sequence shown in Figure 53 (SEQ ID NO:99) evidences the presence of the following: a signal peptide from about amino acid 1 to about amino acid 25, a transmembrane domain from about amino acid 155 to about amino acid 174, a potential N-glycosylation site from about amino acid 196 to about amino acid  
 30 199 and FKBP-type peptidyl-prolyl cis-trans isomer signature sequences from about amino acid 62 to about amino acid 77, from about amino acid 87 to about amino acid 123 and from about amino acid 128 to about amino acid 141. Clone DNA49143-1429 has been deposited with ATCC on June 23, 1998 and is assigned ATCC deposit no. 203013.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST- sequence  
 35 alignment analysis of the full-length sequence shown in Figure 53 (SEQ ID NO:99), evidenced homology between the PRO535 amino acid sequence and the following Dayhoff sequences: S71237, P\_R93551, P\_R28980, S71238, FKB2\_HUMAN, CELC05C8\_1, S55383, S72485, CELC50F2\_6 and S75144.

**EXAMPLE 25: Isolation of cDNA clones Encoding Human PRO718**

A cDNA sequence isolated in the amylase screen described in Example 2 (human fetal lung library) above is herein designated DNA43512 (see Figure 62; SEQ ID NO:108). The DNA43512 sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (LIFESEQ™, Incyte Pharmaceuticals, Palo Alto, CA) to  
 5 identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altschul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into consensus DNA sequences with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated DNA45625. Proprietary  
 10 Genentech EST sequences were employed in the assembly and are herein shown in Figures 58-61.

Based on the DNA45625 sequence, oligonucleotide probes were generated and used to screen a human fetal lung library (LIB25) prepared as described in paragraph 1 of Example 2 above. The cloning vector was pRK5B (pRK5B is a precursor of pRK5D that does not contain the SfiI site; see, Holmes et al., Science, 253:1278-1280 (1991)), and the cDNA size cut was less than 2800 bp.

15 PCR primers (forward and reverse) were synthesized:

forward PCR primer 5'-GGGTGGATGGTACTGCTGCATCC-3' (SEQ ID NO:109)

reverse PCR primer 5'-TGTTGTGCTGTGGGAAATCAGATGTG-3' (SEQ ID NO:110)

Additionally, a synthetic oligonucleotide hybridization probe was constructed from the DNA45625 sequence which had the following nucleotide sequence:

20 hybridization probe

5'-GTGTCTGGAGGCTGTGGCCGTTTGTCTTGGGCTAAAATCGGG-3' (SEQ ID NO:111)

In order to screen several libraries for a source of a full-length clone, DNA from the libraries was screened by PCR amplification with the PCR primer pair identified above. A positive library was then used to isolate clones encoding the PRO718 gene using the probe oligonucleotide and one of the PCR primers.

25 A full length clone was identified that contained a single open reading frame with an apparent translational initiation site at nucleotide positions 36-38 and ending at the stop codon found at nucleotide positions 607-609 (Figure 56; SEQ ID NO:102). The predicted polypeptide precursor is 157 amino acids long, has a calculated molecular weight of approximately 17,400 daltons and an estimated pI of approximately 5.78. Analysis of the full-length PRO718 sequence shown in Figure 57 (SEQ ID NO:103) evidences the presence of  
 30 the following: a type II transmembrane domain from about amino acid 21 to about amino acid 40, and other transmembrane domains at about amino acid 58 to about amino acid 78, about amino acid 95 to about amino acid 114, and about amino acid 127 to about amino acid 147; a cell attachment sequence from about amino acid 79 to about amino acid 81; and a potential N-glycosylation site from about amino acid 53 to about amino acid 56. Clone DNA49647-1398 has been deposited with ATCC on June 2, 1998 and is assigned ATCC deposit no.  
 35 209919.

Analysis of the amino acid sequence of the full-length PRO718 polypeptide suggests that it possesses no significant sequence similarity to any known protein. However, an analysis of the Dayhoff database (version

35.45 SwissProt 35) evidenced some degree of homology between the PRO718 amino acid sequence and the following Dayhoff sequences: AF045606\_1, AF039906\_1, SPBC8D2\_2, S63441, F64728, COX1\_TRYBB, F64375, E64173, RPYGJT\_3, MTCY261\_23.

**EXAMPLE 26: Isolation of cDNA clones Encoding Human PRO872**

5 Use of the signal sequence algorithm described in Example 3 above allowed identification of a single Incyte EST sequence designated herein as clu120709.init. The clu120709.init sequence was then compared a proprietary EST DNA database (LIFESEQ™, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altschul et al., Methods in Enzymology, 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or  
10 in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated DNA48254.

In light of an observed sequence homology between the DNA48254 consensus sequence and an EST sequence encompassed within the Incyte EST clone no. 3438068, the Incyte EST clone 3438068 was purchased  
15 and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein. The sequence of this cDNA insert is shown in Figure 63 and is the full-length DNA sequence for PRO872. Clone DNA49819-1439 was deposited with the ATCC on June 2, 1998, and is assigned ATCC deposit no. 209931.

The entire nucleotide sequence of DNA49819-1439 is shown in Figure 63 (SEQ ID NO:112). Clone  
20 DNA49819-1439 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 14-16 and ending at the stop codon at nucleotide positions 1844-1846 (Figure 63). The predicted polypeptide precursor is 610 amino acids long (Figure 64). The full-length PRO872 protein shown in Figure 64 has an estimated molecular weight of about 66,820 daltons and a pI of about 8.65. Analysis of the full-length PRO872 sequence shown in Figure 64 (SEQ ID NO:113) evidences the presence of the following features: a  
25 signal peptide at amino acid 1 to about 18, putative transmembrane domains at about amino acids 70-87, 200-222 and 568-588; sequence identity with bacterial-type phytoene dehydrogenase protein at about amino acids 71-105; sequence identity with a regulator of chromosome condensation (RCC1) signature 2 at about amino acids 201-211; leucine zipper patterns at about amino acids 214-235, 221-242, 228-249 and 364-385; a potential N-glycosylation site at about amino acids 271-274; and a glycosaminoglycan attachment site at about amino acids  
30 75-78. Analysis of the amino acid sequence of the full-length PRO872 polypeptide using the Dayhoff database (version 35.45 SwissProt 35) evidenced homology between the PRO872 amino acid sequence and the following Dayhoff sequences: PRCRTI\_1, S75951, S74689, CELF37C4\_3, CRTI\_RHOCA, S76617, YNI2\_METTL, MTV014\_14, AOFB\_HUMAN, and MMU70429\_1.

**EXAMPLE 27: Isolation of cDNA clones Encoding Human PRO1063**

35 Use of the signal sequence algorithm described in Example 3 above allowed identification of a single Incyte EST cluster sequence designated herein as ss.clu119743.init. The Incyte EST cluster sequence

ss.clu119743.init sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (LIFESEQ™, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altschul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated DNA48288.

In light of an observed sequence homology between the DNA48288 consensus sequence and an EST sequence encompassed within the Incyte EST clone no. 2783726, the Incyte EST clone 2783726 was purchased and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein. The sequence of this cDNA insert is shown in Figure 65 and is herein designated DNA49820-1427.

The full length clone shown in Figure 65 contained a single open reading frame with an apparent translational initiation site at nucleotide positions 90-92 and ending at the stop codon found at nucleotide positions 993-995 (Figure 65; SEQ ID NO:114). The predicted polypeptide precursor is 301 amino acids long, has a calculated molecular weight of approximately 33,530 daltons and an estimated pI of approximately 4.80. Analysis of the full-length PRO1063 sequence shown in Figure 66 (SEQ ID NO:115) evidences the presence of the following: a signal peptide from about amino acid 1 to about amino acid 21, potential N-glycosylation sites from about amino acid 195 to about amino acid 198, from about amino acid 217 to about amino acid 220 and from about amino acid 272 to about amino acid 275, a glycosaminoglycan attachment site from about amino acid 267 to about amino acid 270, a microbodies C-terminal targeting signal site from about amino acid 299 to about amino acid 301, a type II fibronectin collagen-binding domain homology sequence from about amino acid 127 to about amino acid 168 and a fructose-bisphosphate aldolase class II protein homology sequence from about amino acid 101 to about amino acid 118. Clone DNA49820-1427 has been deposited with the ATCC on June 2, 1998 and is assigned ATCC deposit no. 209932.

Analysis of the amino acid sequence of the full-length PRO1063 polypeptide suggests that it possesses sequence similarity to the human type IV collagenase protein. More specifically, an analysis of the Dayhoff database (version 35.45 SwissProt 35) evidenced some degree of homology between the PRO1063 amino acid sequence and the following Dayhoff sequences, S68303, CFU68533\_1, P\_P91139, RNU65656\_1, PA2R\_RABIT, MMU56734\_1, FINC\_XENLA, A48925, P\_R92778 and FA12\_HUMAN.

#### EXAMPLE 28: Isolation of cDNA clones Encoding Human PRO619

Use of the signal sequence algorithm described in Example 3 above allowed identification of an EST cluster sequence from the Incyte database, designated herein as 88434. This EST cluster sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (LIFESEQ®, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altschul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score

of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington).

In light of an observed sequence homology between the consensus sequence and an EST sequence encompassed within the Incyte EST clone no. 1656694, the Incyte EST clone 1656694 was purchased and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein. The sequence of this cDNA insert is shown in Figure 67 and is herein designated as DNA49821-1562.

The full length clone shown in Figure 67 contained a single open reading frame with an apparent translational initiation site at nucleotide positions 81-83 and ending at the stop codon found at nucleotide positions 450-452 (Figure 67; SEQ ID NO:116). The predicted polypeptide precursor (Figure 68, SEQ ID NO:117) is 123 amino acids long including a predicted signal peptide at about amino acids 1-20. PRO619 has a calculated molecular weight of approximately 13,710 daltons and an estimated pI of approximately 5.19. Clone DNA49821-1562 was deposited with the ATCC on June 16, 1998 and is assigned ATCC deposit no. 209981.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST-2 sequence alignment analysis of the full-length sequence shown in Figure 68 (SEQ ID NO:117), revealed significant homology between the PRO619 amino acid sequence and the following Dayhoff sequences: S35302, D87009\_1, HSU93494\_1, HUMIGLAM5\_1, D86999\_2, HUMIGLYM1\_1, HUMIGLYMKE\_1, A29491\_1, A29498\_1, and VPR2\_MOUSE.

#### EXAMPLE 29: Isolation of cDNA clones Encoding Human PRO943

A consensus DNA sequence encoding PRO943 was assembled relative to other EST sequences using phrap as described in Example 1 above. This consensus sequence was then extended using repeated cycles of BLAST and phrap to extend the consensus sequence as far as possible using the sources of EST sequences discussed above. The extended consensus sequence is herein designated DNA36360. Based on the DNA36360 consensus sequence, oligonucleotides were synthesized: 1) to identify by PCR a cDNA library that contained the sequence of interest, and 2) for use as probes to isolate a clone of the full-length coding sequence for PRO943.

PCR primers (forward and reverse) were synthesized:

forward PCR primer 5'-CGAGATGACGCCGAGCCCC-3' (SEQ ID NO:120)

reverse PCR primer 5'-CGGTTTCGACACGCGGCAGGTG-3' (SEQ ID NO:121)

Additionally, a synthetic oligonucleotide hybridization probe was constructed from the consensus DNA36360 sequence which had the following nucleotide sequence

hybridization probe

5'-TGCTGCTCCTGCTGCCGCCGCTGCTGCTGGGGCCCTCCCGCCGG-3' (SEQ ID NO:122)

In order to screen several libraries for a source of a full-length clone, DNA from the libraries was screened by PCR amplification with the PCR primer pair identified above. A positive library was then used to isolate clones encoding the PRO943 gene using the probe oligonucleotide and one of the PCR primers. RNA for construction of the cDNA libraries was isolated from human fetal brain tissue.

DNA sequencing of the clones isolated as described above gave the full-length DNA sequence for PRO943 (designated herein as DNA52192-1369 [Figure 69, SEQ ID NO:118]) and the derived protein sequence for PRO943.

The entire nucleotide sequence of DNA52192-1369 is shown in Figure 69 (SEQ ID NO:118). Clone DNA52192-1369 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 150-152 and ending at the stop codon at nucleotide positions 1662-1664 (Figure 69). The predicted polypeptide precursor is 504 amino acids long (Figure 70). The full-length PRO943 protein shown in Figure 70 has an estimated molecular weight of about 54,537 daltons and a pI of about 10.04. Analysis of the full-length PRO943 sequence shown in Figure 70 (SEQ ID NO:119) evidences the presence of the following: a signal peptide from about amino acid 1 to about amino acid 17, a transmembrane domain from about amino acid 376 to about amino acid 396, tyrosine kinase phosphorylation sites from about amino acid 212 to about amino acid 219 and from about amino acid 329 to about amino acid 336, potential N-glycosylation sites from about amino acid 111 to about amino acid 114, from about amino acid 231 to about amino acid 234, from about amino acid 255 to about amino acid 258 and from about amino acid 293 to about amino acid 296 and an immunoglobulin and MHC protein sequence homology block from about amino acid 219 to about amino acid 236. Clone DNA52192-1369 has been deposited with ATCC on July 1, 1998 and is assigned ATCC deposit no. 203042.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST-2 sequence alignment analysis of the full-length sequence shown in Figure 70 (SEQ ID NO:119), evidenced significant homology between the PRO943 amino acid sequence and the following Dayhoff sequences: B49151, A39752, FGR1\_XENLA, S38579, RATHBFGFRB\_1, TVHU2F, FGR2\_MOUSE, CEK3\_CHICK, P\_R21080 and A27171\_1.

#### EXAMPLE 30: Isolation of cDNA clones Encoding Human PRO1188

A consensus DNA sequence was assembled relative to other EST sequences using the program "phrap" as described in Example 1 above. This consensus sequence is designated herein as DNA45679. Based on the DNA45679 consensus sequence, oligonucleotides were synthesized: 1) to identify by PCR a cDNA library that contained the sequence of interest, and 2) for use as probes to isolate a clone of the full-length coding sequence for PRO1188.

PCR primers (forward and reverse) were synthesized:

forward PCR primer 5'-CTGGTGCCTCAACAGGGAGCAG-3' (SEQ ID NO:125)

reverse PCR primer 5'-CCATTGTGCAGGTCAGGTCACAG-3' (SEQ ID NO:126)

Additionally, a synthetic oligonucleotide hybridization probe was constructed from the consensus DNA45679 sequence which had the following nucleotide sequence:

hybridization probe

5'-CTGGAGCAAGTGCTCAGCTGCCTGTGGTCAGACTGGGGTC-3' (SEQ ID NO:127)

In order to screen several libraries for a source of a full-length clone, DNA from the libraries was screened by PCR amplification with the PCR primer pair identified above. A positive library was then used to isolate clones encoding the PRO1188 gene using the probe oligonucleotide and one of the PCR primers. RNA

for construction of the cDNA libraries was isolated from human fetal kidney tissue.

DNA sequencing of the clones isolated as described above gave the full-length DNA sequence for PRO1188 (designated herein as DNA52598-1518 [Figure 71, SEQ ID NO:123]); and the derived protein sequence for: PRO1188.

The entire coding sequence of PRO1188 is shown in Figure 71 (SEQ ID NO:123). Clone DNA52598-1518 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 136-138 and an apparent stop codon at nucleotide positions 3688-3690. The predicted polypeptide precursor is 1184 amino acids long. The full-length PRO1188 protein shown in Figure 72 has an estimated molecular weight of about 132,582 Daltons and a pI of about 8.80. Additional features include: a signal peptide at about amino acids 1-31; an ATP/GTP binding site motif A (P-loop) at about amino acids 266-273; an aldehyde dehydrogenases cysteine active site at about amino acids 188-199; growth factor and cytokines receptors family signature 2 at about amino acids 153-159; and potential N-glycosylation sites at about amino acids 129-132, 132-135, 346-349, 420-423, 550-553, 631-634, 1000-1003, and 1056-1059.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST-2 sequence alignment analysis of the full-length sequence shown in Figure 72 (SEQ ID NO:124), revealed significant homology between the PRO1188 amino acid sequence and the following Dayhoff sequences: SSU83114\_1, S56015, CET21B6\_4, CELT19D2\_1, and TSP1\_MOUSE.

Clone DNA52598-1518 has been deposited with ATCC and is assigned ATCC deposit no 203107.

#### EXAMPLE 31: Isolation of cDNA clones Encoding Human PRO1133

A consensus DNA sequence was assembled relative to other EST sequences using phrap as described in Example 1 above. This sequence was extended using repeated cycles of phrap. The extended consensus sequence is designated herein DNA38102. Based on the DNA38102 consensus sequence, oligonucleotides were synthesized: 1) to identify by PCR a cDNA library that contained the sequence of interest, and 2) for use as probes to isolate a clone of the full-length coding sequence for PRO1133.

PCR primers (two forward and one reverse) were synthesized:

forward PCR primer 1 5'-TCGATTATGGACGAACATGGCAGC-3' (SEQ ID NO:130);

forward PCR primer 2 5'-TTCTGAGATCCCTCATCCTC-3' (SEQ ID NO:131); and

reverse primer 5'-AGGTTTCAGGGACAGCAAGTTTGGG-3' (SEQ ID NO:132).

Additionally, a synthetic oligonucleotide hybridization probe was constructed from the consensus DNA38102 sequence which had the following nucleotide sequence:

hybridization probe

5'TTTGCTGGACCTCGGCTACGGAATTGGCTTCCCTCTACGGACAGCTGGAT3' (SEQ ID NO:133).

In order to screen several libraries for a source of a full-length clone, DNA from the libraries was screened by PCR amplification with a PCR primer pair identified above. A positive library was then used to isolate clones encoding the PRO1133 gene using the probe oligonucleotide and one of the PCR primers. RNA for construction of the cDNA libraries was isolated from human fetal kidney tissue.



DNA sequencing of the clones isolated as described above gave the full-length DNA sequence for PRO1133 and the derived protein sequence for PRO1133.

The entire coding sequence of PRO1133 is shown in Figure 73 (SEQ ID NO:128). Clone DNA53913-1490 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 266-268 and an apparent stop codon at nucleotide positions 1580-1582 of SEQ ID NO:128. The predicted polypeptide precursor is 438 amino acids long. The signal peptide is at amino acids 1-18 of SEQ ID NO:129. EGF-like domain cysteine pattern signatures start at 315 and 385 of SEQ ID NO:129 as shown in Figure 74. Clone DNA53913-1490 has been deposited with ATCC and is assigned ATCC deposit no. 203162. The full-length PRO1133 protein shown in Figure 74 has an estimated molecular weight of about 49,260 daltons and a pI of about 6.15.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST-2 sequence alignment analysis of the full-length sequence shown in Figure 74 (SEQ ID NO:129), revealed some sequence identity between the PRO1133 amino acid sequence and the following Dayhoff sequences (data from the database incorporated herein): AF002717\_1, LMG1\_HUMAN, B54665, UNC6\_CAEEL, LML1\_CAEEL, LMA5\_MOUSE, MMU88353\_1, LMA1\_HUMAN, HSLN2C64\_1 and AF005258\_1.

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#### EXAMPLE 32: Isolation of cDNA clones Encoding Human PRO784

An initial DNA sequence (SEQ ID NO:136), referred to herein as DNA44661 and shown in Figure 77, was identified using a yeast screen, in a human fetal lung cDNA library that preferentially represents the 5' ends of the primary cDNA clones. DNA44661 was then compared to ESTs from public databases (e.g., GenBank), and a proprietary EST database (LIFESEQ®, Incyte Pharmaceuticals, Palo Alto, CA), using the computer program BLAST or BLAST2 [Altschul et al., *Methods in Enzymology*, 266:460-480 (1996)]. The ESTs were then clustered and assembled into a consensus DNA sequence using the computer program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained is designated herein as "DNA45463". Based on the DNA45463 consensus sequence, oligonucleotides were synthesized for use as probes to isolate a clone of the full-length coding sequence for PRO784 from a human fetal lung cDNA library.

The full length DNA53978-1443 clone shown in Figure 75 contained a single open reading frame with an apparent translational initiation site at nucleotide positions 37-39 and ending at the stop codon found at nucleotide positions 821-823 (Figure 75; SEQ ID NO:134). The predicted polypeptide precursor (Figure 76, SEQ ID NO:135) is 228 amino acids long. PRO784 has a calculated molecular weight of approximately 25,735 Daltons and an estimated pI of approximately 5.45. PRO784 has the following features: a signal peptide at about amino acid 1 to about 15; transmembrane domains at about amino acids 68 to about 87 and at about 183 to about 204; potential N-myristoylation sites at about amino acids 15-20, 51-56, 66-60, 163-168, and 206-211; and an RNP-1 protein RNA-binding region at about amino acids 108 to about 117.

Clone DNA53978-1443 was deposited with ATCC on June 16, 1998, and is assigned ATCC deposit no. 209983.

Based on a BLAST and FastA sequence alignment analysis (using the ALIGN computer program) of the full-length sequence, PRO784 shows amino acid sequence identity to the following proteins: RNU42209\_1,

MMU91538\_1, CGU91742\_1, CELF55A4\_6, SC22\_YEAST, and F48188.

EXAMPLE 33: Isolation of cDNA Clones Encoding Human PRO783

A yeast screening assay was employed to identify cDNA clones that encoded potential secreted proteins. Use of this yeast screening assay allowed identification of a single cDNA clone, designated herein as DNA45201 (Figure 80; SEQ ID NO:139).

The DNA45201 sequence was then used to search expressed sequence tag (EST) databases for the presence of potential homologies. The EST databases included public EST databases (e.g., GenBank) and a proprietary EST DNA database (LIFESEQ™, Incyte Pharmaceuticals, Palo Alto, CA). The search was performed using the computer program BLAST or BLAST2 (Altschul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, Univ. of Washington, Seattle, Washington). The consensus sequence obtained is herein designated as "consen01". A proprietary Genentech EST sequence was used in the consensus assembly and is herein designated as DNA14575 (Figure 81; SEQ ID NO:140).

Based on the consen01 sequence, oligonucleotides were synthesized: 1) to identify by PCR a cDNA library that contained the sequence of interest, and 2) for use as probes to isolate a clone of the full-length coding sequence for PRO783. In order to screen several libraries for a full-length clone, DNA from the libraries was screened by PCR amplification, as per Ausubel et al., Current Protocols in Molecular Biology, with the PCR primer pair. A positive library was then used to isolate clones encoding the gene of interest using the probe oligonucleotide and one of the primer pairs.

PCR primers (forward and reverse) were synthesized:

forward PCR primer 5'-GACTGTATCTGAGCCCCAGACTGC-3' (SEQ ID NO:141),

forward PCR primer 5'-TCAGCAATGAGGTGCTGCTC-3' (SEQ ID NO:142), and

reverse PCR primer 5'-TGAGGAAGATGAGGGACAGGTTGG-3' (SEQ ID NO:143).

Additionally, a synthetic oligonucleotide hybridization probe was constructed from the consen01 sequence which had the following nucleotide sequence:

hybridization probe

5'-TATGGAAGCACCTGACTACGAAGTGCTATCCGTGCGAGAACAGCTATTCC-3' (SEQ ID NO:144).

In order to screen several libraries for a source of a full-length clone, DNA from the libraries was screened by PCR amplification with a PCR primer pair identified above. A positive library was then used to isolate clones encoding the PRO783 gene using the probe oligonucleotide and one of the PCR primers.

RNA for construction of the cDNA libraries was isolated from human fetal kidney tissue (LIB228). The cDNA libraries used to isolate the cDNA clones were constructed by standard methods using commercially available reagents such as those from Invitrogen, San Diego, CA. The cDNA was primed with oligo dT containing a NotI site, linked with blunt to SalI hemikinased adaptors, cleaved with NotI, sized appropriately by gel electrophoresis, and cloned in a defined orientation into a suitable cloning vector (such as pRKB or pRKD; pRK5B is a precursor of pRK5D that does not contain the SfiI site; see, Holmes et al., Science,

253:1278-1280 (1991)) in the unique XhoI and NotI sites.

DNA sequencing of the clones isolated as described above gave the full-length DNA sequence for PRO783 [herein designated as DNA53996-1442] (SEQ ID NO:137) and the derived protein sequence for PRO783.

The entire nucleotide sequence of DNA53996-1442 is shown in Figure 78 (SEQ ID NO:137). Clone  
 5 DNA53996-1442 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 310-312 and ending at the stop codon at nucleotide positions 1777-1779 (Figure 78). The predicted polypeptide precursor is 489 amino acids long (Figure 79). The full-length PRO783 protein shown in Figure 79 has an estimated molecular weight of about 55,219 daltons and a pI of about 8.47. Analysis of the full-length PRO783 sequence shown in Figure 79 (SEQ ID NO:138) evidences the presence of the following features:  
 10 transmembrane domains located at about amino acids 23-42, 67-89, 111-135, 154-176, 194-218, 296-319, 348-370, 387-410 and 427-452; leucine zipper patterns located at about amino acids 263-283 and 399-420; a potential tyrosine kinase phosphorylation site at about amino acids 180-187; potential N-glycosylation sites at about amino acids 105 -108 and 121-124; potential cAMP- and a cGMP-dependent protein kinase phosphorylation site at about amino acids 288-291; and a region having sequence identity with bacterial  
 15 rhodopsins retinal binding site protein at about amino acids 190-218.

An analysis of the Dayhoff database (version 35.45 SwissProt 35) shows some sequence identity between the PRO783 amino acid sequence and the following Dayhoff sequences: YNC2\_CAEEL, D64048, ATAC002332\_3F4P9.3, NY2R\_SHEEP, and VSH\_MUMPA.

Clone DNA53996-1442 was deposited with the ATCC on June 2, 1998, and is assigned ATCC deposit  
 20 no. 209921.

#### EXAMPLE 34: Isolation of cDNA Clones Encoding Human PRO820

An expressed sequence tag (EST) DNA database (Merck/Wash. U) was searched and an EST designated  
 EST no. AA504080, Merck clone 825136, was identified (library 312, human B-cell tonsil). Homology searches  
 25 revealed that this EST showed sequence identity with low affinity immunoglobulin gamma Fc receptor II. DNA sequencing gave the full-length DNA sequence for PRO820 and the derived protein sequence for PRO820.

The entire nucleotide sequence of DNA56041-1416 is shown in Figure 82 (SEQ ID NO:145). Clone  
 DNA56041-1416 contains a single open reading frame with an apparent translational initiation site at nucleotide  
 30 positions 115-117 and ending at the stop codon at nucleotide positions 487-489 (Figure 82). The predicted polypeptide precursor is 124 amino acids long (Figure 83). The full-length PRO820 protein shown in Figure 83 has an estimated molecular weight of about 14,080 daltons and a pI of about 7.48. Clone DNA56041-1416 has been deposited with ATCC. Regarding the sequence, it is understood that the deposited clone contains the correct sequence, and the sequences provided herein are based on known sequencing techniques.

Still analyzing the amino acid sequence of SEQ ID NO:146, the putative signal peptide is at about amino  
 35 acids 1-15 of SEQ ID NO:146. Protein kinase C phosphorylation sites are at about amino acids 20-22 and 43-45 of SEQ ID NO:146. An N-myristoylation site is at about amino acids 89-94 of SEQ ID NO:146. An immunoglobulin and major histocompatibility complex domain is at about amino acids 83-90 of SEQ ID NO:146.

The corresponding nucleotides can be routinely determined given the sequences provided herein.

**EXAMPLE 35: Isolation of cDNA Clones Encoding Human PRO1080**

A consensus DNA sequence was assembled relative to other EST sequences using phrap and was extended using repeated cycles of BLAST and phrap so as to extend the consensus sequence as far as possible using the sources of the EST sequences as described in Example 1 above. The consensus sequence is designated herein as DNA52640. An EST proprietary to Genentech was employed in the consensus assembly and is herein designated as DNA36527 (Figure 86; SEQ ID NO:149).

In light of an observed sequence homology between the DNA36527 consensus sequence and an EST sequence encompassed within the Merck EST clone no. 526423, the Merck EST clone 526423 was purchased and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein. The sequence of this cDNA insert is shown in Figure 84 and is herein designated as DNA56047-1456.

The entire nucleotide sequence of DNA56047-1456 is shown in Figure 84 (SEQ ID NO:147). Clone DNA56047-1456 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 159-161 and ending at the stop codon at nucleotide positions 1233-1235 of SEQ ID NO:147 (Figure 84). The predicted polypeptide precursor is 358 amino acids long (Figure 85). The full-length PRO1080 protein shown in Figure 85 has an estimated molecular weight of about 40,514 daltons and a pI of about 6.08. Clone DNA56047-1456 has been deposited with ATCC on June 9, 1998. It is understood that the deposited clone has the actual nucleic acid sequence and that the sequences provided herein are based on known sequencing techniques.

Also shown in Figure 85 are the approximate locations of the signal peptide, cell attachment site, Nt-DnaJ domain signature, region having sequence identity with Nt-DnaJ domain proteins, and N-glycosylation sites. The corresponding nucleic acids of these amino acid sequences and others provided herein can be routinely determined by the information provided herein.

**EXAMPLE 36: Isolation of cDNA Clones Encoding Human PRO1079**

A consensus DNA sequence was assembled relative to other EST sequences using phrap as described in Example 1 above, and is herein designated DNA52714. Based on information provided by the assembly, the clone for Merck EST no. HO6898 was obtained and sequenced, thereby giving the nucleotide sequence designated herein as DNA56050-1455. The entire nucleotide sequence of DNA56050-1455 is shown in Figure 87 (SEQ ID NO:150). Clone DNA56050-1455 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 183-185 and ending at the stop codon at nucleotide positions 861-863 (Figure 87). The predicted polypeptide precursor is 226 amino acids long (Figure 88). The full-length PRO1079 protein shown in Figure 88 has an estimated molecular weight of about 24,611 Daltons and a pI of about 4.85. Analysis of the full-length PRO1079 sequence shown in Figure 88 (SEQ ID NO:3) evidences the presence of the following features: a signal peptide at about amino acid 1-29; potential N-myristoylation sites at about amino acids 10-15, and 51-56; homology to photosystem I psaG and psaK proteins at about amino acids 2 to 20; and homology to prolyl endopeptidase family serine proteins at about amino acids 150 to 163.

Analysis of the amino acid sequence of the full-length PRO1079 polypeptide using the Dayhoff database (version 35.45 SwissProt 35) evidenced some sequence identity between the PRO1079 amino acid sequence and the following Dayhoff sequences: CEK10C3\_4, MMU50734\_1, D69503, AF051149\_1, and VSMP\_CVMS.

Clone UNQ536 (DNA56050-1455) was deposited with the ATCC on June 22, 1998, and is assigned ATCC deposit no. 203011.

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#### EXAMPLE 37: Isolation of cDNA clones Encoding Human PRO793

A cDNA clone (DNA56110-1437) encoding a native human PRO793 polypeptide was identified by a yeast screen, in a human skin tumor cDNA library that preferentially represents the 5' ends of the primary cDNA clones. The yeast screen employed identified a single EST clone designated herein as DNA50177 (Figure 91; SEQ ID NO:154). The DNA50177 sequence was then compared to various EST databases including public EST databases (e.g., GenBank), and a proprietary EST database (LIFESEQ<sup>®</sup>, Incyte Pharmaceuticals, Palo Alto, CA) to identify homologous EST sequences. The comparison was performed using the computer program BLAST or BLAST2 [Altschul et al., *Methods in Enzymology*, 266:460-480 (1996)]. Those comparisons resulting in a BLAST score of 70 (or in some cases, 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). This consensus sequence is herein designated DNA50972.

In light of an observed sequence homology between the DNA50972 consensus sequence and an EST sequence encompassed within the Merck EST clone no. N33874, the Merck EST clone N33874 was purchased and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein. The sequence of this cDNA insert is shown in Figure 89 and is herein designated as DNA56110-1437.

The full-length DNA56110-1437 clone shown in Figure 89 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 77-79 and ending at the stop codon at nucleotide positions 491-493 (Figure 89). The predicted polypeptide precursor is 138 amino acids long (Figure 90). The full-length PRO793 protein shown in Figure 90 has an estimated molecular weight of about 15,426 daltons and a pI of about 10.67. Analysis of the full-length PRO793 sequence shown in Figure 90 (SEQ ID NO:153) evidences the presence of the following: transmembrane domains from about amino acid 12 to about amino acid 30, from about amino acid 33 to about amino acid 52, from about amino acid 69 to about amino acid 89 and from about amino acid 93 to about amino acid 109, potential N-myristoylation sites from about amino acid 11 to about amino acid 16, from about amino acid 51 to about amino acid 56 and from about amino acid 116 to about amino acid 121 and an amino acid sequence block having homology to an aminoacyl-transfer RNA synthetase class-II protein from about amino acid 49 to about amino acid 59. Clone DNA56110-1437 has been deposited with ATCC on August 11, 1998 and is assigned ATCC deposit no. 203113.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST-2 sequence alignment analysis of the full-length sequence shown in Figure 90 (SEQ ID NO:153), evidenced certain homology between the PRO793 amino acid sequence and the following Dayhoff sequences: S47453, AF015193\_12, MTEHGNS9\_2, E64030, H69784, D64995, CD53\_MOUSE, GEN8006, AE001138\_7 and COX2\_STRPU.

**EXAMPLE 38: Isolation of cDNA Clones Encoding Human PRO1016**

A consensus DNA sequence was assembled relative to other EST sequences using phrap as described in Example 1 above. The consensus sequence obtained is herein designated DNA53502.

In light of an observed sequence homology between the DNA53502 consensus sequence and an EST sequence encompassed within the Merck EST clone no. 38680, the Merck EST clone 38680 was purchased and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein. The sequence of this cDNA insert is shown in Figure 92.

The entire nucleotide sequence of DNA56113-1378 is shown in Figure 92 (SEQ ID NO:155). Clone DNA56113-1378 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 168-170 and ending at the stop codon at nucleotide positions 1302-1304 (Figure 92). The predicted polypeptide precursor is 378 amino acids long (Figure 93). The full-length PRO1016 protein shown in Figure 93 has an estimated molecular weight of about 44,021 daltons and a pI of about 9.07. Clone DNA56113-1378 has been deposited with the ATCC. Regarding the sequence, it is understood that the deposited clone contains the correct sequence, and the sequences provided herein are based on known sequencing techniques.

Analysis of the amino acid sequence of the full-length PRO1016 polypeptide suggests that portions of it possess sequence identity with acyltransferase, thereby indicating that PRO1016 may be a novel acyltransferase.

Still analyzing the amino acid sequence of SEQ ID NO:156, the putative signal peptide is at about amino acids 1-18 of SEQ ID NO:156. The transmembrane domain(s) are at about amino acids 332-352 and 305-330 of SEQ ID NO:156. The fructose-bisphosphate aldolase class-II protein homology sequence is at about amino acids 73-90 of SEQ ID NO:156. The extradiol ring-cleavage dioxygenase protein is at about amino acids 252-275 of SEQ ID NO:156. The corresponding nucleotides can be routinely determined given the sequences provided herein.

The specific Dayhoff database designation names of sequences to which PRO1016 has sequence identity with include the following: S52645, P\_R59712, P\_R99249, P\_R59713, BNAGPATRF\_1, CELT05H4\_15 and CELZK40\_1.

**EXAMPLE 39: Isolation of cDNA Encoding Human PRO1013**

A consensus DNA sequence was assembled relative to other EST sequences using phrap as described in Example 1 above. The consensus DNA sequence was then extended using repeated cycles of BLAST and phrap to extend the consensus sequence as far as possible using the sources of EST sequences.

In light of an observed sequence homology between the consensus sequence and an EST sequence encompassed within the Incyte EST clone no. 3107695, the Incyte EST clone 3107695 was purchased and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein. The sequence of this cDNA insert is shown in Figure 94 and is herein designated as DNA56410-1414.

The entire nucleotide sequence of DNA56410-1414 is shown in Figure 94 (SEQ ID NO:157). Clone DNA56410-1414 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 17-19 and ending at the stop codon at nucleotide positions 1244-1246 (Figure 94). The predicted

polypeptide precursor is 409 amino acids long (Figure 95). The full-length PRO1013 protein shown in Figure 95 has an estimated molecular weight of about 46,662 daltons and a pI of about 7.18. Clone DNA56410-1414 has been deposited with the ATCC. Regarding the sequence, it is understood that the deposited clone contains the correct sequence, and the sequences provided herein are based on known sequencing techniques.

5 Still analyzing the amino acid sequence of SEQ ID NO:158, the putative signal peptide is at about amino acids 1-19 of SEQ ID NO:158. N-glycosylation sites are at about amino acids 75-78 and 322-325 of SEQ ID NO:158. An N-myristoylation site is at about amino acids 184-189 of SEQ ID NO:158. A growth factor and cytokine receptor family domain is at about amino acids 134-149 of SEQ ID NO:158. The corresponding nucleotides can be routinely determined given the sequences provided herein.

10 Blast analysis showed some sequence identity with other proteins. Specifically, PRO1013 has some sequence identity with at least the Dayhoff sequences designated: D63877\_1; MHU22019\_1, AE000730\_10, and AF019079\_1.

#### EXAMPLE 40: Isolation of cDNA Clones Encoding Human PRO937

15 A consensus DNA sequence was assembled relative to other EST sequences using phrap as described in Example 1 above. That consensus sequence is herein designated DNA49651. Based on the DNA49651 consensus sequence, oligonucleotides were synthesized: 1) to identify by PCR a cDNA library that contained the sequence of interest, and 2) for use as probes to isolate a clone of the full-length coding sequence for PRO937.

PCR primers (forward and reverse) were synthesized:

20 forward PCR primer 5'-CTCCGTGGTAAACCCACAGCCC-3' (SEQ ID NO:161); and  
reverse PCR primer 5'-TCACATCGATGGGATCCATGACCG-3' (SEQ ID NO:162).

Additionally, a synthetic oligonucleotide hybridization probe was constructed from the DNA48651 sequence which had the following nucleotide sequence:

25 hybridization probe  
 5'-GGTCTCGTGACTGTGAAGCCATGTTACAACACTACTGCTCAAACATCATGAG-3' (SEQ ID NO:163).

In order to screen several libraries for a source of a full-length clone, DNA from the libraries was screened by PCR amplification with the PCR primer pair identified above. A positive library was then used to isolate clones encoding the PRO937 gene using the probe oligonucleotide and one of the PCR primers. RNA for construction of the cDNA libraries was isolated from human fetal kidney tissue (LIB227).

30 DNA sequencing of the clones isolated as described above gave the full-length DNA sequence for PRO937 [herein designated as DNA56436-1448] (SEQ ID NO:159) and the derived protein sequence for PRO937.

The entire nucleotide sequence of DNA56436-1448 is shown in Figure 96 (SEQ ID NO:159). It contains a single open reading frame having an apparent translational initiation site at nucleotide positions 499-501 and ending at the stop codon found at nucleotide positions 2167-2169 (Figure 96, SEQ ID NO:159). The predicted polypeptide precursor is 556 amino acids long, has a calculated molecular weight of approximately 62,412 daltons and an estimated pI of approximately 6.62. Analysis of the full-length PRO937 sequence shown

in Figure 97 (SEQ ID NO:160) evidences the presence of the following features: signal peptide at about amino acids 1-22; ATP/GTP-binding site motif A (P-loop) at about amino acids 515-523; a potential N-glycosylation site at about amino acids 514-517; and sites of glypican homology at about amino acids 54-74, 106-156, 238-279, 309-345, 423-459, and 468-505.

5 Clone DNA56436-1448 has been deposited with ATCC on May 27, 1998, and is assigned ATCC deposit no. 209902.

Analysis of the amino acid sequence of the full-length PRO937 polypeptide suggests that it possesses significant sequence similarity to glypican proteins, thereby indicating that PRO937 may be a novel glypican protein. More specifically, an analysis of the Dayhoff database (version 35.45 SwissProt 35) evidenced significant homology between the PRO937 amino acid sequence and the following Dayhoff sequences:

10 GPCCK\_MOUSE, GPC2\_RAT, GPC5\_HUMAN, GPC3\_HUMAN, P\_R30168, CEC03H12\_2, GEN13820, HS119E23\_1, HDAC\_DROME, and AF017637\_1.

#### EXAMPLE 41: Isolation of cDNA clones Encoding Human PRO842

Use of the signal sequence algorithm described in Example 3 above allowed identification of a single

15 Incyte EST cluster sequence designated herein as Incyte EST cluster sequence no. 69572. This EST cluster sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (LIFESEQ®, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altschul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a

20 BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated DNA54230.

In light of an observed sequence homology between the consensus sequence and an EST sequence encompassed within the Merck EST clone no. AA477092, the Merck EST clone AA477092 was purchased and

25 the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein. The sequence of this cDNA insert is shown in Figure 98 and is herein designated as DNA56855-1447.

The full length clone shown in Figure 98 contained a single open reading frame with an apparent translational initiation site at nucleotide positions 153-155 and ending at the stop codon found at nucleotide positions 510-512 (Figure 98; SEQ ID NO:164). The predicted polypeptide precursor (Figure 99, SEQ ID

30 NO:165) is 119 amino acids long. PRO842 has a calculated molecular weight of approximately 13,819 Daltons and an estimated pI of approximately 11.16. Other features of PRO842 include a signal peptide at about amino acids 1-22, a potential protein kinase C phosphorylation site at about amino acids 39-41 and two potential N-myristoylation sites at about amino acids 27-32 and about amino acids 46-51.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST-2 sequence

35 alignment analysis of the full-length sequence shown in Figure 98 (SEQ ID NO:164), evidenced some homology between the PRO842 amino acid sequence and the following Dayhoff sequences: CEZK131\_1, P\_R80843, RAT5HT2X\_1, S81882\_1, A60912, MCU60315\_137MC137L, U93422\_1, p\_P91996, U93462\_1, and



## ZN18\_HUMAN.

Clone DNA56855-1447 was deposited with the ATCC on June 23, 1998, and is assigned ATCC deposit no. 203004.

EXAMPLE 42: Isolation of cDNA clones Encoding Human PRO839

5 Use of the signal sequence algorithm described in Example 3 above allowed identification of an EST cluster sequence from the Incyte LIFESEQ® database, designated Incyte EST Cluster No. 24479. This EST cluster sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (LIFESEQ®, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using  
10 the computer program BLAST or BLAST2 (Altschul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated DNA55709.

15 In light of an observed sequence homology between the DNA55709 consensus sequence and an EST sequence encompassed within the Merck EST clone no. 754525, the Merck EST clone 754525 was purchased and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein. The sequence of this cDNA insert is shown in Figure 100 and is herein designated as DNA56859-1445.

The full length clone shown in Figure 100 contained a single open reading frame with an apparent  
20 translational initiation site at nucleotide positions 2-4 and ending at the stop codon found at nucleotide positions 263-265 (Figure 100; SEQ ID NO:166). The predicted polypeptide precursor (Figure 101, SEQ ID NO:167) is 87 amino acids long. PRO839 has a calculated molecular weight of approximately 9,719 Daltons and an estimated pI of approximately 4.67. Other features of PRO839 include a signal peptide at about amino acids 1-23, potential protein kinase C phosphorylation sites at about amino acids 37-39 and about amino acids 85-87,  
25 a potential casein kinase II phosphorylation site at about amino acids 37-40, sequence identity with ribonucleotide reductase large subunit protein at about amino acids 50-60, and sequence identity with eukaryotic RNA-binding region RNP-1 proteins at about amino acids 70-79.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST-2 sequence alignment analysis of the full-length sequence shown in Figure 101 (SEQ ID NO:167), evidenced some  
30 homology between the PRO839 amino acid sequence and the following Dayhoff sequences: CD14\_MOUSE, XPR6\_YARLI, HS714385\_1, S49783, BB19\_RABIT, GVPH-HALME, AB003135\_1, P\_R85453, LUU27081\_2, and TP2B\_MOUSE.

Clone DNA56859-1445 was deposited with the ATCC on June 23, 1998, and is assigned ATCC deposit no.209019.

35

**EXAMPLE 43: Isolation of cDNA Clones Encoding Human PRO1180**

Use of the signal sequence algorithm described in Example 3 above allowed identification of a single Incyte EST cluster sequence (Incyte EST cluster sequence no. 14732). The Incyte EST cluster sequence no. 14732 sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (LIFESEQ™, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altschul et al., *Methods in Enzymology* 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated DNA55711.

- 5 In light of an observed sequence homology between the DNA55711 consensus sequence and an EST sequence encompassed within the Merck EST clone no. T60981, the Merck EST clone T60981 was purchased and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein. The sequence of this cDNA insert is shown in Figure 102 and is herein designated DNA56860-1510.

- 15 The full length clone shown in Figure 102 contained a single open reading frame with an apparent translational initiation site at nucleotide positions 78-80 and ending at the stop codon found at nucleotide positions 909-911 (Figure 102; SEQ ID NO:168). The predicted polypeptide precursor is 277 amino acids long, has a calculated molecular weight of approximately 31,416 daltons and an estimated pI of approximately 8.88. Analysis of the full-length PRO1180 sequence shown in Figure 103 (SEQ ID NO:169) evidences the presence of the following: a signal peptide from about amino acid 1 to about amino acid 23, a leucine zipper pattern sequence from about amino acid 10 to about amino acid 31, and potential N-myristoylation sited from about amino acid 64 to about amino acid 69, from about amino acid 78 to about amino acid 83, from about amino acid 80 to about amino acid 85, from about amino acid 91 to about amino acid 96 and from about amino acid 201 to about amino acid 206. Clone DNA56860-1510 has been deposited with the ATCC on June 9, 1998 and is assigned ATCC deposit no. 209952.

- 25 Analysis of the amino acid sequence of the full-length PRO1180 polypeptide suggests that it possesses sequence similarity to the methyltransferase family of proteins. More specifically, an analysis of the Dayhoff database (version 35.45 SwissProt 35) evidenced some degree of homology between the PRO1180 amino acid sequence and the following Dayhoff sequences, MTC165\_14, D69267, YH09\_YEAST, BIOC\_SERMA, ATAC00448415T1D16.16, SHGCPIR\_18, SPBC3B9\_4, AB009504\_14, P\_W17977 and A69952.

30

**EXAMPLE 44: Isolation of cDNA clones Encoding Human PRO1134**

Use of the signal sequence algorithm described in Example 3 above allowed identification of an EST cluster sequence from the Incyte database, designated 7511. This EST cluster sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (Lifeseq®, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altschul et al., *Methods in Enzymology* 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or

35

in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated DNA55725. Two proprietary Genentech EST sequences were employed in the assembly and are shown in Figure 106 (SEQ ID NO:172) and Figure 107 (SEQ ID NO:173).

5 In light of an observed sequence homology between the DNA55725 consensus sequence and an EST sequence encompassed within the Merck EST clone no. H94897, the Merck EST clone H94897 was purchased and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein. The sequence of this cDNA insert is shown in Figure 106 and is herein designated as DNA56865-1491.

10 Clone DNA56865-1491 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 153-155 and ending at the stop codon at nucleotide positions 1266-1268 (Figure 104). The predicted polypeptide precursor is 371 amino acids long (Figure 105). The full-length PRO1134 protein shown in Figure 105 has an estimated molecular weight of about 41,935 daltons and a pI of about 9.58. Analysis of the full-length PRO1134 sequence shown in Figure 105 (SEQ ID NO:171) evidences the presence of the following: a signal peptide from about amino acid 1 to about amino acid 23, potential N-glycosylation sites from  
15 about amino acid 103 to about amino acid 106, from about amino acid 249 to about amino acid 252 and from about amino acid 257 to about amino acid 260, and an amino acid block having homology to tyrosinase CuA-binding region proteins from about amino acid 280 to about amino acid 306. Clone DNA56865-1491 has been deposited with ATCC on June 23, 1998 and is assigned ATCC deposit no. 203022.

20 An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST-2 sequence alignment analysis of the full-length sequence shown in Figure 105 (SEQ ID NO:171), evidenced significant homology between the PRO1134 amino acid sequence and the following Dayhoff sequences: F20P5\_18, AC002396\_10, S47847, C64146, GSPA\_BACSU, P\_W10564, RFAI\_ECOLI, Y258\_HAEIN, RFAJ\_SALTY and P\_R32985.

#### 25 EXAMPLE 45: Isolation of cDNA clones Encoding Human PRO830

Use of the signal sequence algorithm described in Example 3 above allowed identification of an EST cluster sequence from the Incytedatabase, designated 20251. This EST cluster sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (LIFESEQ®, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing  
30 homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altschul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated DNA55733.

35 In light of an observed sequence homology between the DNA55733 consensus sequence and an EST sequence encompassed within the Merck EST clone no. H78534, the Merck EST clone H78534 was purchased and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein.

The sequence of this cDNA insert is shown in Figure 108 and is herein designated as DNA56866-1342.

Clone DNA56866-1342 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 154-156 and ending at the stop codon at nucleotide positions 415-417 (Figure 108). The predicted polypeptide precursor is 87 amino acids long (Figure 109). The full-length PRO830 protein shown in Figure 109 has an estimated molecular weight of about 9,272 daltons and a pI of about 9.19. Analysis of the full-length PRO830 sequence shown in Figure 109 (SEQ ID NO:175) evidences the presence of the following:

a signal peptide from about amino acid 1 to about amino acid 33, potential N-myristoylation sites from about amino acid 2 to about amino acid 7 and from about amino acid 8 to about amino acid 13 and a thioredoxin family of proteins homology block from about amino acid 23 to about amino acid 39. Clone UNQ470 (DNA56866-1342) has been deposited with ATCC on June 22, 1998 and is assigned ATCC deposit no. 203023.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST-2 sequence alignment analysis of the full-length sequence shown in Figure 109 (SEQ ID NO:175), evidenced significant homology between the PRO830 amino acid sequence and the following Dayhoff sequences: HSU88154\_1, HSU88153\_1, SAPKSGENE\_1, HPU31791\_5, GGCNOT2\_1, CPU91421\_1, CHKESTPC09\_1, PQ0769, U97553\_79 and B60095.

#### EXAMPLE 46: Isolation of cDNA clones Encoding Human PRO1115

Use of the signal sequence algorithm described in Example 3 above allowed identification of an EST cluster sequence from the LIFESEQ® database, designated Incyte EST cluster sequence no. 165008. This EST cluster sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (LIFESEQ®, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altschul et al., *Methods in Enzymology* 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated DNA55726.

In light of an observed sequence homology between the DNA55726 consensus sequence and an EST sequence encompassed within the Merck EST clone no. R75784, the Merck EST clone R75784 was purchased and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein.

The sequence of this cDNA insert is shown in Figure 111 and is herein designated as DNA56868-1478.

The full length clone shown in Figure 110 contained a single open reading frame with an apparent translational initiation site at nucleotide positions 189-191 and ending at the stop codon found at nucleotide positions 1524-1526 (Figure 110; SEQ ID NO:176). The predicted polypeptide precursor (Figure 111, SEQ ID NO:177) is 445 amino acids long. PRO1115 has a calculated molecular weight of approximately 50,533 Daltons and an estimated pI of approximately 8.26. Additional features include a signal peptide at about amino acids 1-20; potential N-glycosylation sites at about amino acids 204-207, 295-298, and 313-316; and putative transmembrane domains at about amino acids 35-54, 75-97, 126-146, 185-204, 333-350, and 353-371.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST-2 sequence alignment analysis of the full-length sequence shown in Figure 111 (SEQ ID NO:177), evidenced some amino acid sequence identity between the PRO1115 amino acid sequence and the following Dayhoff sequences: AF053947\_79, S73698, CEC47A10\_4, CCOMTNDSSG\_1, HS4LMP2AC\_1, LMP2\_EBV, PA24\_MOUSE, HCU33331\_7, P-W05508, and AF002273\_1.

- 5        Clone DNA56868-1478 was deposited with the ATCC on June 23, 1998 and is assigned ATCC deposit no. 203024..

EXAMPLE 47: Isolation of cDNA clones Encoding Human PRO1277

- 10        A consensus DNA sequence was assembled relative to other ESTs using repeated cycles of BLAST and the program "phrap" as described in Example 1 above. One or more of the ESTs from the assembly was derived from diseased coronary artery tissue. The consensus sequence obtained is designated herein as "DNA49434".

- 15        In light of an observed sequence homology between the DNA49434 consensus sequence and an EST sequence encompassed within the Incyte EST clone no. 3042605, the Incyte EST clone 3042605 was purchased and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein. The sequence of this cDNA insert is shown in Figure 112 (SEQ ID NO:178).

- 20        Clone DNA56869-1545 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 188-190, and an apparent stop codon at nucleotide positions 2222-2224 (Figure 112). The predicted polypeptide precursor is 678 amino acids long (Figure 113). The full-length PRO1277 protein shown in Figure 113 has an estimated molecular weight of about 73,930 daltons and a pI of about 9.48. Additional features include a signal peptide at about amino acids 1-26; a transmembrane domain at about amino acids 181-200, and potential N-glycosylation sites at about amino acids 390-393 and 520-523.

- 25        An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST-2 sequence alignment analysis of the full-length sequence shown in Figure 113 (SEQ ID NO:179), revealed significant homology between the PRO1277 amino acid sequence and Dayhoff sequence no AF012252\_1. Homology was also found between the PRO1277 amino acid sequence and the following Dayhoff sequences: AF006740\_1, CA36\_HUMAN, HSU1\_1, HUMCOL7A1X\_1, CA17\_HUMAN, MMZ78163\_1, CAMA\_CHICK, HSU69263\_1, YNX3\_CAEEL, and MMRNAM3\_1.

- 30        Clone DNA56869-1545 has been deposited with ATCC and is assigned ATCC deposit no. 203161.

EXAMPLE 48: Isolation of cDNA Clones Encoding Human PRO1135

- 35        A consensus DNA sequence was assembled relative to other EST sequences using phrap as described in Example 1 above. This consensus sequence is herein designated DNA52767. Based on the DNA52767 consensus sequence, oligonucleotides were synthesized: 1) to identify by PCR a cDNA library that contained the sequence of interest, and 2) for use as probes to isolate a clone of the full-length coding sequence for PRO1135.

In order to screen several libraries for a source of a full-length clone, DNA from the libraries was screened by PCR amplification with PCR primer pairs prepared based upon the DNA52767 sequence. A positive library was then used to isolate clones encoding the PRO1135 gene using the probe oligonucleotide and one of the PCR primers. RNA for construction of the cDNA libraries was isolated from human coronary artery smooth muscle tissue (LIB309). The cDNA libraries used to isolate the cDNA clones were constructed by standard methods using commercially available reagents such as those from Invitrogen, San Diego, CA. The cDNA was primed with oligo dT containing a NotI site, linked with blunt to SalI hemikinased adaptors, cleaved with NotI, sized appropriately by gel electrophoresis, and cloned in a defined orientation into a suitable cloning vector (such as pRKB or pRKD; pRK5B is a precursor of pRK5D that does not contain the SfiI site; see, Holmes et al., *Science*, 253:1278-1280 (1991)) in the unique XhoI and NotI sites.

DNA sequencing of the clones isolated as described above gave the full-length DNA sequence for PRO1135 [herein designated as DNA56870-1492] (SEQ ID NO:180) and the derived protein sequence for PRO1135.

The entire nucleotide sequence of DNA56870-1492 is shown in Figure 114 (SEQ ID NO:180). Clone DNA56870-1492 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 62-64 and ending at the stop codon at nucleotide positions 1685-1687 (Figure 114). The predicted polypeptide precursor is 541 amino acids long (Figure 115). The full-length PRO1135 protein shown in Figure 115 has an estimated molecular weight of about 60,335 daltons and a pI of about 5.26. Analysis of the full-length PRO1135 sequence shown in Figure 115 (SEQ ID NO:181) evidences the presence of the following: a signal peptide from about amino acid 1 to about amino acid 21, potential N-glycosylation sites from about amino acid 53 to about amino acid 56, from about amino acid 75 to about amino acid 78, from about amino acid 252 to about amino acid 255 and from about amino acid 413 to about amino acid 416 and an amino acid block having homology to glycosyl hydrolase family 35 proteins from about amino acid 399 to about amino acid 414. Clone DNA56870-1492 has been deposited with ATCC on June 2, 1998 and is assigned ATCC deposit no. 209925.

Analysis of the amino acid sequence of the full-length PRO1135 polypeptide suggests that it possesses significant sequence similarity to the alpha 1,2-mannosidase protein, thereby indicating that PRO1135 may be a novel mannosidase. More specifically, an analysis of the Dayhoff database (version 35.45 SwissProt 35) evidenced significant homology between the PRO1135 amino acid sequence and the following Dayhoff sequences, DMC86E4\_5, D86967\_1, SPAC23A1\_4, YH04\_YEAST, B54408, SSMAN9MAN\_1, CEZC410\_4, S61631 and MSU14190\_1.

#### EXAMPLE 49: Isolation of cDNA Clones Encoding Human PRO114

A cDNA sequence isolated in the amylase screen described in Example 2 above was found, by the WU-BLAST-2 sequence alignment computer program, to have certain sequence identity to other known interferon receptors. This cDNA sequence is herein designated DNA48466 and is shown in Figure 118 (SEQ ID NO:184). Based on the sequence identity, probes were generated from the sequence of the DNA48466 molecule and used to screen a human breast carcinoma library (LIB135) prepared as described in paragraph 1 of Example 2 above. The cloning vector was pRK5B (pRK5B is a precursor of pRK5D that does not contain the SfiI site; see, Holmes

et al., *Science*, 253:1278-1280 (1991)), and the cDNA size cut was less than 2800 bp.

The oligonucleotide probes employed were as follows:

forward PCR primer 5'-AGGCTTCGCTGCGACTAGACCTC-3' (SEQ ID NO:185)

reverse PCR primer 5'-CCAGGTCGGGTAAGGATGGTTGAG-3' (SEQ ID NO:186)

hybridization probe

- 5 5'-TTTCTACGCATTGATTCCATGTTTGCTCACAGATGAAGTGGCCATTCTGC-3' (SEQ ID NO:187)

A full length clone was identified that contained a single open reading frame with an apparent translational initiation site at nucleotide positions 250-252, and a stop signal at nucleotide positions 1183-1185 (Figure 116, SEQ ID NO:182). The predicted polypeptide precursor is 311 amino acids long, has a calculated molecular weight of approximately 35,076 daltons and an estimated pI of approximately 5.04. Analysis of the full-length PRO1114 interferon receptor sequence shown in Figure 117 (SEQ ID NO:183) evidences the presence of the following: a signal peptide from about amino acid 1 to about amino acid 29, a transmembrane domain from about amino acid 230 to about amino acid 255, potential N-glycosylation sites from about amino acid 40 to about amino acid 43 and from about amino acid 134 to about amino acid 137, an amino acid sequence block having homology to tissue factor proteins from about amino acid 92 to about amino acid 119 and an amino acid sequence block having homology to integrin alpha chain proteins from about amino acid 232 to about amino acid 262. Clone DNA57033-1403 has been deposited with ATCC on May 27, 1998 and is assigned ATCC deposit no. 209905.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST-2 sequence alignment analysis of the full-length sequence shown in Figure 117 (SEQ ID NO:183), evidenced significant homology between the PRO1114 interferon receptor amino acid sequence and the following Dayhoff sequences: G01418, INR1\_MOUSE, P\_R71035, INGS\_HUMAN, A26595\_1, A26593\_1, I56215 and TF\_HUMAN.

#### EXAMPLE 50: Isolation of cDNA Clones Encoding Human PRO828

A consensus DNA sequence was identified using the method described in Example 1 above. This consensus sequence is herein designated DNA35717. Based on the DNA35717 consensus sequence, oligonucleotides were synthesized: 1) to identify by PCR a cDNA library that contained the sequence of interest, and 2) for use as probes to isolate a clone of the full-length coding sequence for PRO828.

PCR primers (forward and reverse) were synthesized:

forward PCR primer 5'-GCAGGACTTCTACGACTTCAAGGC-3' (SEQ ID NO:190); and

- 30 reverse PCR primer 5'-AGTCTGGGCCAGGTACTTGAAGGC-3' (SEQ ID NO:191).

Additionally, a synthetic oligonucleotide hybridization probe was constructed from the consensus DNA35717 sequence which had the following nucleotide sequence:

hybridization probe

- 5'-CAACATCCGGGGCAAACCTGGTGTGCTGGAGAAGTACCGCGGATCGGTGT-3' (SEQ ID NO:192)

In order to screen several libraries for a source of a full-length clone, DNA from the libraries was screened by PCR amplification with the PCR primer pair identified above. A positive library was then used to isolate clones encoding the PRO828 gene using the probe oligonucleotide and one of the PCR primers. RNA

for construction of the cDNA libraries was isolated from human fetal lung tissue (LIB25).

DNA sequencing of the clones isolated as described above gave the full-length DNA sequence for PRO828 [herein designated as DNA57037-1444] (SEQ ID NO:188) and the derived protein sequence for PRO828.

The entire nucleotide sequence of DNA57037-1444 is shown in Figure 119 (SEQ ID NO:188). Clone  
 5 DNA57037-1444 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 34-36 and ending at the stop codon at nucleotide positions 595-597 (Figure 119). The predicted polypeptide precursor is 187 amino acids long (Figure 120). The full-length PRO828 protein shown in Figure 120 has an estimated molecular weight of about 20,996 daltons and a pI of about 8.62. Analysis of the full-length PRO828 sequence shown in Figure 120 (SEQ ID NO:189) evidences the presence of the following: a  
 10 signal peptide at about amino acids 1- 21; sequences identity to glutathione peroxidases signature 2 at about amino acids 82-89; sequence identity to glutathione peroxidases selenocysteine proteins at about amino acids 35-60, 63-100, 107-134, and 138-159. Clone DNA57037-1444 has been deposited with ATCC on May 27, 1998, and is assigned ATCC deposit no. 209903.

Analysis of the amino acid sequence of the full-length PRO828 polypeptide suggests that it possesses  
 15 significant sequence similarity to glutathione peroxidases, thereby indicating that PRO828 may be a novel peroxidase enzyme. More specifically, an analysis of the Dayhoff database (version 35.45 SwissProt 35) evidenced sequence identity between the PRO828 amino acid sequence and the following Dayhoff sequences: AF053311\_1, CELT09A12\_2, AC004151\_3, BTUE\_ECOLI, CER05H10\_3, P\_P80918, PWU88907\_1, and P\_W22308.

20

#### EXAMPLE 51: Isolation of cDNA clones Encoding Human PRO1009

A cDNA clone (DNA57129-1413) encoding a native human PRO1009 polypeptide was identified by the use of a yeast screen, in a human SK-Lu-1 adenocarcinoma cell line cDNA library that preferentially represents the 5' ends of the primary cDNA clones. First SEQ ID NO:195 (Figure 123) was identified, which  
 25 was extended by alignments to other EST sequences to form a consensus sequence. Oligonucleotide probes based upon the consensus sequence were synthesized and used to screen the cDNA library which gave rise to the full-length DNA57129-1413 clone.

The full length DNA57129-1413 clone shown in Figure 121 contained a single open reading frame with an apparent translational initiation site at nucleotide positions 41-43 and ending at the stop codon found at  
 30 nucleotide positions 1886-1888 (Figure 121; SEQ ID NO:193). The predicted polypeptide precursor (Figure 122, SEQ ID NO:194) is 615 amino acids long. Figure 122 also shows the approximate locations of the signal sequence, transmembrane domains, myristoylation sites, a glycosylation site and an AMP-binding domain. PRO1009 has a calculated molecular weight of approximately 68,125 daltons and an estimated pI of approximately 7.82. Clone DNA57129-1413 has been deposited with ATCC and is assigned ATCC deposit no.  
 35 209977. It is understood that the deposited clone has the actual and correct sequence and that the representations herein may have minor, normal sequencing errors.



Based on a WU-BLAST-2 sequence alignment analysis (using the ALIGN computer program) of the full-length sequence, PRO1009 shows amino acid sequence identity to at least the following proteins which were designated in a Dayhoff database as follows: F69893, CEF28F8\_2, BSY13917\_7, BSY13917\_7, D69187, D69649, XCRPFB\_1, E64928, YDID\_ECOLI, BNACSF8\_1 and RPU75363\_2.

5 **EXAMPLE 52: Isolation of cDNA Clones Encoding Human PRO1007**

A consensus DNA sequence was assembled relative to other EST sequences using phrap as described in Example 1 above. This consensus sequence is herein designated as DNA40671.

In light of an observed sequence homology between the DNA40671 consensus sequence and an EST sequence encompassed within the Merck EST clone no. T70513, the Merck EST clone T70513 was purchased  
10 and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein. The sequence of this cDNA insert is shown in Figure 124.

The entire nucleotide sequence of DNA57690-1374 is shown in Figure 124 (SEQ ID NO:196). Clone DNA57690-1374 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 16-18 and ending at the stop codon at nucleotide positions 1054-1056 (Figure 124). The predicted  
15 polypeptide precursor is 346 amino acids long (Figure 125). The full-length PRO1007 protein shown in Figure 125 has an estimated molecular weight of about 35,971 daltons and a pI of about 8.17. Clone DNA57690-1374 has been deposited with the ATCC on June 9, 1998. Regarding the sequence, it is understood that the deposited clone contains the actual sequence, and the sequences provided herein are based on known sequencing techniques. The representative figures herein show the representative numbering.

20 Analysis of the amino acid sequence of the full-length PRO1007 polypeptide suggests that portions of it possess sequence identity to MAGPIAP, thereby indicating that PRO1007 may be a novel member of the family to which MAGPIAP belongs.

Still analyzing the amino acid sequence of SEQ ID NO:197, the putative signal peptide is at about amino acids 1-30 of SEQ ID NO:197. The transmembrane domain is at amino acids 325-346 of SEQ ID NO:197. N-  
25 glycosylation sites are at about amino acids 118-121, 129-132, 163-166, 176-179, 183-186 and 227-130 of SEQ ID NO:197. Ly-6/u-Par domain protein homology is at about amino acids 17-36 and 209-222 of SEQ ID NO:197. The corresponding nucleotides of the amino acids presented herein can be routinely determined given the sequences provided herein.

30 **EXAMPLE 53: Isolation of cDNA clones Encoding Human PRO1056**

Use of the signal sequence algorithm described in Example 3 above allowed identification of an EST cluster sequence from the Incyte database, designated herein as 6425. This EST cluster sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (Lifeseq®, Incyte Pharmaceuticals, Palo Alto, CA) to identify  
35 existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altschul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a

consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated DNA55736.

In light of an observed sequence homology between the DNA55736 consensus sequence and an EST sequence encompassed within the Merck EST clone no. R88049, the Merck EST clone R88049 was purchased and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein.

- 5 The sequence of this cDNA insert is shown in Figure 126 and is herein designated as DNA57693-1424.

Clone DNA57693-1424 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 56-58 and ending at the stop codon at nucleotide positions 416-418 (Figure 126). The predicted polypeptide precursor is 120 amino acids long (Figure 127). The full-length PRO1056 protein shown in Figure 127 has an estimated molecular weight of about 13,345 daltons and a pI of about 5.18. Analysis of the full-length PRO1056 sequence shown in Figure 127 (SEQ ID NO:199) evidences the presence of the following: a signal peptide from about amino acid 1 to about amino acid 18, a transmembrane domain from about amino acid 39 to about amino acid 58, a potential N-glycosylation site from about amino acid 86 to about amino acid 89, protein kinase C phosphorylation sites from about amino acid 36 to about amino acid 38 and from about amino acid 58 to about amino acid 60, a tyrosine kinase phosphorylation site from about amino acid 25 to about amino acid 32 and an amino acid sequence block having homology to channel forming colicin proteins from about amino acid 24 to about amino acid 56. Clone DNA57693-1424 has been deposited with ATCC on June 23, 1998 and is assigned ATCC deposit no. 203008.

- 10 An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST-2 sequence alignment analysis of the full-length sequence shown in Figure 127 (SEQ ID NO:199), evidenced significant homology between the PRO1056 amino acid sequence and the following Dayhoff sequences: PLM\_HUMAN, A40533, ATNG\_HUMAN, A55571, ATNG\_SHEEP, S31524, GEN13025, RIC\_MOUSE, A48678 and A10871\_1.

#### EXAMPLE 54: Isolation of cDNA clones Encoding Human PRO826

- 25 Use of the signal sequence algorithm described in Example 3 above allowed identification of an EST cluster sequence from the Incyte database, designated 47283. This EST cluster sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (LIFESEQ®, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altschul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated DNA56000.

- 35 In light of an observed sequence homology between the DNA56000 consensus sequence and an EST sequence encompassed within the Merck EST clone no. W69233, the Merck EST clone W69233 was purchased and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein. The sequence of this cDNA insert is shown in Figure 128 and is herein designated as DNA57694-1341.

Clone DNA57694-1341 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 13-15 and ending at the stop codon at nucleotide positions 310-312 (Figure 128). The predicted polypeptide precursor is 99 amino acids long (Figure 129). The full-length PRO826 protein shown in Figure 129 has an estimated molecular weight of about 11,050 daltons and a pI of about 7.47. Analysis of the full-length PRO826 sequence shown in Figure 129 (SEQ ID NO:201) evidences the presence of the following: a signal peptide from about amino acid 1 to about amino acid 22, potential N-myristoylation sites from about amino acid 22 to about amino acid 27 and from about amino acid 90 to about amino acid 95 and an amino acid sequence block having homology to peroxidase from about amino acid 16 to about amino acid 48. Clone DNA57694-1341 has been deposited with ATCC on June 22, 1998 and is assigned ATCC deposit no. 203017.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST-2 sequence alignment analysis of the full-length sequence shown in Figure 129 (SEQ ID NO:201), evidenced significant homology between the PRO826 amino acid sequence and the following Dayhoff sequences: CCU12315\_1, SCU96108\_6, CELF39F10\_4 and HELT\_HELHO.

#### EXAMPLE 55: Isolation of cDNA clones Encoding Human PRO819

Use of the signal sequence algorithm described in Example 3 above allowed identification of an EST cluster sequence from the Incyte database, designated 49605. This EST cluster sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (LIFESEQ®, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altschul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated DNA56015.

In light of an observed sequence homology between the DNA56015 consensus sequence and an EST sequence encompassed within the Merck EST clone no. H65785, the Merck EST clone H65785 was purchased and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein. The sequence of this cDNA insert is shown in Figure 130 and is herein designated as DNA57695-1340.

Clone DNA57695-1340 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 46-48 and ending at the stop codon at nucleotide positions 202-204 (Figure 130). The predicted polypeptide precursor is 52 amino acids long (Figure 131). The full-length PRO819 protein shown in Figure 131 has an estimated molecular weight of about 5,216 daltons and a pI of about 4.67. Analysis of the full-length PRO819 sequence shown in Figure 131 (SEQ ID NO:203) evidences the presence of the following: a signal peptide from about amino acid 1 to about amino acid 24, a potential N-myristoylation site from about amino acid 2 to about amino acid 7 and a region having homology to immunoglobulin light chain from about amino acid 5 to about amino acid 33. Clone DNA57695-1340 has been deposited with ATCC on June 23, 1998 and is assigned ATCC deposit no. 203006.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 131 (SEQ ID NO:203), evidenced significant homology between the PRO819 amino acid sequence and the following Dayhoff sequences: HSU03899\_1, HUMIGLITEB\_1, VG28\_HSVSA, AF031522\_1, PAD1\_YEAST and AF045484\_1.

5 EXAMPLE 56: Isolation of cDNA Clones Encoding Human PRO1006

An initial candidate sequence from Incyte cluster sequence no. 45748 was identified using the signal algorithm process described in Example 3 above. This sequence was then aligned with a variety of public and Incyte EST sequences and a consensus sequence designated herein as DNA56036 was derived therefrom.

10 In light of an observed sequence homology between the DNA56036 consensus sequence and an EST sequence encompassed within the Merck EST clone no. 489737, the Merck EST clone 489737 was purchased and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein. The sequence of this cDNA insert is shown in Figure 132.

The entire nucleotide sequence of DNA57699-1412 is shown in Figure 132 (SEQ ID NO:204). Clone DNA57699-1412 contains a single open reading frame with an apparent translational initiation site at nucleotide  
15 positions 28-30 and ending at the stop codon at nucleotide positions 1204-1206 (Figure 132). The predicted polypeptide precursor is 392 amino acids long (Figure 133). The full-length PRO1006 protein shown in Figure 133 has an estimated molecular weight of about 46,189 daltons and a pI of about 9.04. Clone DNA57699-1412 has been deposited with the ATCC. Regarding the sequence, it is understood that the deposited clone contains the correct sequence, and the sequences provided herein are based on known sequencing techniques.

20 Analyzing the amino acid sequence of SEQ ID NO:205, the putative signal peptide is at about amino acids 1-23 of SEQ ID NO:205. The N-glycosylation sites are at about amino acids 40-43, 53-56, 204-207 and 373-376 of SEQ ID NO:205. An N-myristoylation site is at about amino acids 273-278 of SEQ ID NO:205.

The corresponding nucleotides of these amino acid regions and others can be routinely determined given the sequences provided herein.

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EXAMPLE 57: Isolation of cDNA Clones Encoding Human PRO1112

Use of the signal sequence algorithm described in Example 3 above allowed identification of a specific EST cluster sequence. This EST cluster sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database  
30 (LIFESEQ<sup>®</sup>, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altschul et al., *Methods in Enzymology* 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is  
35 herein designated DNA56018.

In light of an observed sequence homology between the DNA56018 consensus sequence and an EST sequence encompassed within the Merck EST clone no. AA223546, the Merck EST clone AA223546 was

purchased and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein. The sequence of this cDNA insert is shown in Figure 134 and is herein designated as DNA57702-1476.

The entire nucleotide sequence of DNA57702-1476 is shown in Figure 134 (SEQ ID NO:206). Clone DNA57702-1476 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 20-22 and ending at the stop codon at nucleotide positions 806-808 of SEQ ID NO:206 (Figure 134).

- 5 The predicted polypeptide precursor is 262 amino acids long (Figure 135). The full-length PRO1112 protein shown in Figure 135 has an estimated molecular weight of about 29,379 daltons and a pI of about 8.93. Figure 135 also shows the approximate locations of the signal peptide and transmembrane domains. Clone DNA57702-1476 has been deposited with the ATCC on June 9, 1998. It is understood that the deposited clone has the actual nucleic acid sequence and that the sequences provided herein are based on known sequencing techniques.

- 10 Analysis of the amino acid sequence of the full-length PRO1112 polypeptide suggests that it possesses some sequence similarity to other proteins. More specifically, an analysis of the Dayhoff database (version 35.45 SwissProt 35) evidenced some sequence identity between the PRO1112 amino acid sequence and at least the following Dayhoff sequences, MTY20B11\_13 (a mycobacterium tuberculosis peptide), F64471, AE000690\_6, XLU16364\_1, E43259 (H<sup>+</sup>-transporting ATP synthase) and PIGSLADRXE\_1 (MHC class II  
15 histocompatibility antigen).

#### EXAMPLE 58: Isolation of cDNA clones Encoding Human PRO1074

- Use of the signal sequence algorithm described in Example 3 above allowed identification of a single Incyte EST cluster sequence (Incyte cluster sequence No. 42586). This cluster sequence was then compared to  
20 a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (LIFESEQ<sup>TM</sup>, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altschul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus  
25 DNA sequence with the program "phrap" (Phil Green, Univ. of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated DNA56251.

- In light of an observed sequence homology between the DNA56251 consensus sequence and an EST sequence encompassed within the Merck EST clone no. AA081912, the Merck EST clone AA081912 was purchased and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length  
30 protein. The sequence of this cDNA insert is shown in Figure 136 and is the full-length DNA sequence for PRO1074. Clone DNA57704-1452 was deposited with the ATCC on June 9, 1998, and is assigned ATCC deposit no. 209953.

- The entire nucleotide sequence of DNA57704-1452 is shown in Figure 136 (SEQ ID NO:208). Clone DNA57704-1452 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 322-324 and ending at the stop codon at nucleotide positions 1315-1317 (Figure 136). The predicted  
35 polypeptide precursor is 331 amino acids long (Figure 137). The full-length PRO1074 protein shown in Figure 137 has an estimated molecular weight of about 39,512 Daltons and a pI of about 8.03. Analysis of the full-

length PRO1074 sequence shown in Figure 137 (SEQ ID NO:209) evidences the presence of the following features: a transmembrane domain at about amino acids 20 to 39; potential N-glycosylation sites at about amino acids 72 to 75, 154 to 157, 198 to 201, 212 to 215, and 326 to 329; a glycosaminoglycan attachment site at about amino acids 239 to 242, and a Ly-6/u-PAR domain at about amino acids 23 to 36.

Analysis of the amino acid sequence of the full-length PRO1074 polypeptide suggests that it possesses significant sequence similarity to beta 1,3-galactosyltransferase, thereby indicating that PRO1074 may be a novel member of the galactosyltransferase family of proteins. Analysis of the amino acid sequence of the full-length PRO1074 polypeptide using the Dayhoff database (version 35.45 SwissProt 35) evidenced homology between the PRO1074 amino acid sequence and the following Dayhoff sequences: AF029792\_1, P\_R57433, DMU41449\_1, AC000348\_14, P\_R47479, CET09F5\_2, CEF14B6\_4, CET15D6\_5, CEC54C8\_4, and CEE03H4\_10.

Clone DNA57704-1452 was deposited with the ATCC on June 9, 1998, and is assigned ATCC deposit no. 209953.

#### EXAMPLE 59: Isolation of cDNA clones Encoding Human PRO1005

Use of the signal sequence algorithm described in Example 3 above allowed identification of an EST cluster sequence from the LIFESEQ® database, Incyte cluster sequence no. 49243. This EST cluster sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (LIFESEQ®, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altschul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated DNA56380.

In light of an observed sequence homology between the DNA56380 consensus sequence and an EST sequence encompassed within the Merck EST clone no. AA256657, the Merck EST clone AA256657 was purchased and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein. The sequence of this cDNA insert is shown in Figure 138 and is herein designated as DNA57708-1411.

The full length clone shown in Figure 138 contained a single open reading frame with an apparent translational initiation site at nucleotide positions 30-32 and ending at the stop codon found at nucleotide positions 585-587 (Figure 138; SEQ ID NO:210). The predicted polypeptide precursor (Figure 139, SEQ ID NO:211) is 185 amino acids long. PRO1005 has a calculated molecular weight of approximately 20,331 daltons and an estimated pI of approximately 5.85. Clone DNA57708-1411 was deposited with the ATCC June 23, 1998, and is assigned ATCC deposit no. 203021.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 139 (SEQ ID NO:211), evidenced some homology between the PRO1005 amino acid sequence and the following Dayhoff sequences: DDU07187\_1, DDU87912\_1, CELD1007\_14, A42239, DDU42597\_1, CYAG\_DICDI, S50452, MRKC\_KLEPN, P-R41998,

and XYNA\_RUMFL.

**EXAMPLE 60: Isolation of cDNA clones Encoding Human PRO1073**

An initial DNA sequence referred to herein as DNA55938 and shown in Figure 142 (SEQ ID NO:214) was identified using a yeast screen, in a human SK-Lu-1 adenocarcinoma cell line cDNA library that preferentially represents the 5' ends of the primary cDNA clones. DNA55938 was then compared to ESTs from public databases (e.g., GenBank), and a proprietary EST database (LIFESEQ®, Incyte Pharmaceuticals, Palo Alto, CA), using the computer program BLAST or BLAST2 [Altschul et al., *Methods in Enzymology*, 266:460-480 (1996)]. The ESTs were clustered and assembled into a consensus DNA sequence using the computer program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained is designated herein as DNA56411.

In light of an observed sequence homology between the DNA56411 consensus sequence and an EST sequence encompassed within the Merck EST clone no. H86027, the Merck EST clone H86027 was purchased and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein. The sequence of this cDNA insert is shown in Figure 140.

The full length DNA57710-1451 clone shown in Figure 140 contained a single open reading frame with an apparent translational initiation site at nucleotide positions 345-347 and ending at the stop codon found at nucleotide positions 1242-1244 (Figure 140; SEQ ID NO:212). The predicted polypeptide precursor (Figure 141, SEQ ID NO:213) is 299 amino acids long. PRO1073 has a calculated molecular weight of approximately 34,689 daltons and an estimated pI of approximately 11.49. The PRO1073 polypeptide has the following additional features: a signal peptide at about amino acids 1-31, sequence identity to bZIP transcription factor basic domain signature at about amino acids, a potential N-glycosylation site at about amino acids 2-5, and sequence identity with protamine P1 proteins at about amino acids 158-183.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST-2 sequence alignment analysis of the full-length sequence shown in Figure 141 (SEQ ID NO:213), revealed some sequence identity between the PRO1073 amino acid sequence and the following Dayhoff sequences: MMU37351\_1, ATAC00250510T9J22.10, S59043, ENXNUPR\_1, B47328, SR55\_DROME, S26650, SON\_HUMAN, VIT2\_CHICK, and XLC4SRPRT\_1.

Clone DNA57710-1451 was deposited with the ATCC on July 1, 1998 and is assigned ATCC deposit no. 203048.

**EXAMPLE 61: Isolation of cDNA clones Encoding Human PRO1152**

A cDNA clone (DNA57711-1501) encoding a native human PRO1152 polypeptide was identified by employing a yeast screen, in a human infant brain cDNA library that preferentially represents the 5' ends of the primary cDNA clones. Specifically, a yeast screen was employed to identify a cDNA designated herein as DNA55807 (SEQ ID NO:217; see Figure 145).

In light of an observed sequence homology between the DNA55807 sequence and an EST sequence encompassed within the Merck EST clone no. R56756, the Merck EST clone R56756 was purchased and the

cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein. The sequence of this cDNA insert is shown in Figure 143.

The full-length DNA57711-1501 clone shown in Figure 143 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 58-60 and ending at the stop codon at nucleotide positions 1495-1497 (Figure 143). The predicted polypeptide precursor is 479 amino acids long (Figure 144).

- 5 The full-length PRO1152 protein shown in Figure 144 has an estimated molecular weight of about 53,602 daltons and a pI of about 8.82. Analysis of the full-length PRO1152 sequence shown in Figure 144 (SEQ ID NO:216) evidences the presence of the following: a signal peptide from about amino acid 1 to about amino acid 28, transmembrane domains from about amino acid 133 to about amino acid 155, from about amino acid 168 to about amino acid 187, from about amino acid 229 to about amino acid 247, from about amino acid 264 to about amino acid 285, from about amino acid 309 to about amino acid 330, from about amino acid 371 to about amino acid 390 and from about amino acid 441 to about amino acid 464, potential N-glycosylation sites from about amino acid 34 to about amino acid 37 and from about amino acid 387 to about amino acid 390 and an amino acid sequence block having homology to a respiratory-chain NADH dehydrogenase subunit from about amino acid 243 to about amino acid 287. Clone DNA57711-1501 has been deposited with ATCC on July 1, 1998 and is assigned ATCC deposit no. 203047.

- 15 An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST-2 sequence alignment analysis of the full-length sequence shown in Figure 144 (SEQ ID NO:216), evidenced significant homology between the PRO1152 amino acid sequence and the following Dayhoff sequences: AF052239\_1, SYNN9CGA\_1, SFCYTB2\_1, GEN12507, P\_R11769, MTV025\_109, C61168, S43171, P\_P61689 and P\_P61696.

#### EXAMPLE 62: Isolation of cDNA clones Encoding Human PRO1136

- Use of the signal sequence algorithm described in Example 3 above allowed identification of an EST cluster sequence from the Incyte database, designated 109142. This EST cluster sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (Lifeseq®, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altschul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated DNA56039.

- In light of an observed sequence homology between the DNA56039 consensus sequence and an EST sequence encompassed within the Merck EST clone no. HSC1NF011, the Merck EST clone HSC1NF011 was purchased and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein. The sequence of this cDNA insert is shown in Figure 146 and is herein designated as DNA57827-1493.

Clone DNA57827-1493 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 216-218 and ending at the stop codon at nucleotide positions 2112-2114 (Figure 146).



The predicted polypeptide precursor is 632 amino acids long (Figure 147). The full-length PRO1136 protein shown in Figure 147 has an estimated molecular weight of about 69,643 daltons and a pI of about 8.5. Analysis of the full-length PRO1136 sequence shown in Figure 147 (SEQ ID NO:219) evidences the presence of the following: a signal peptide from about amino acid 1 to about amino acid 15 and potential N-glycosylation sites from about amino acid 108 to about amino acid 111, from about amino acid 157 to about amino acid 160, from about amino acid 289 to about amino acid 292 and from about amino acid 384 to about amino acid 387. Clone DNA57827-1493 has been deposited with ATCC on July 1, 1998 and is assigned ATCC deposit no. 203045.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 147 (SEQ ID NO:219), evidenced significant homology between the PRO1136 amino acid sequence and the following Dayhoff sequences: AF034746\_1, AF034745\_1, MMAF000168\_19, HSMUPP1\_1, AF060539\_1, SP97\_RAT, I38757, MMU93309\_1, CEK01A6\_4 and HSA224747\_1.

#### EXAMPLE 63: Isolation of cDNA clones Encoding Human PRO813

Use of the signal sequence algorithm described in Example 3 above allowed identification of a single Incyte EST cluster sequence (Incyte EST cluster sequence no. 45501). The Incyte EST cluster sequence no. 45501 sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (LIFESEQ™, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altschul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated DNA56400.

In light of an observed sequence homology between the DNA56400 consensus sequence and an EST sequence encompassed within the Merck EST clone no. T90592, the Merck EST clone T90592 was purchased and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein. The sequence of this cDNA insert is shown in Figure 148 and is herein designated DNA57834-1339.

The full length clone shown in Figure 148 contained a single open reading frame with an apparent translational initiation site at nucleotide positions 109-111 and ending at the stop codon found at nucleotide positions 637-639 (Figure 149; SEQ ID NO:221). The predicted polypeptide precursor is 176 amino acids long, has a calculated molecular weight of approximately 19,616 daltons and an estimated pI of approximately 7.11. Analysis of the full-length PRO813 sequence shown in Figure 149 (SEQ ID NO:221) evidences the presence of the following: a signal peptide from about amino acid 1 to about amino acid 26 and potential N-myristoylation sites from about amino acid 48 to about amino acid 53, from about amino acid 153 to about amino acid 158, from about amino acid 156 to about amino acid 161 and from about amino acid 167 to about amino acid 172. Clone DNA57834-1339 has been deposited with the ATCC on June 9, 1998 and is assigned ATCC deposit no. 209954.

Analysis of the amino acid sequence of the full-length PRO813 polypeptide suggests that it possesses sequence similarity to the pulmonary surfactant-associated protein C. More specifically, an analysis of the Dayhoff database (version 35.45 SwissProt 35) evidenced some degree of homology between the PRO813 amino acid sequence and the following Dayhoff sequences, P\_SPC\_MUSVI, P\_P92071, G02964, P\_R65489, P\_P82977, P\_R84555, S55542, MUSIGHAJ\_1 and PH1158.

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EXAMPLE 64: Isolation of cDNA Clones Encoding Human PRO809

Use of the signal sequence algorithm described in Example 3 above allowed identification of a single Incyte EST cluster sequence. The Incyte EST cluster sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (LIFESEQ™, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altschul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated DNA56418.

In light of an observed sequence homology between the DNA56418 consensus sequence and an EST sequence encompassed within the Merck EST clone no. H74302, the Merck EST clone H74302 was purchased and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein. The sequence of this cDNA insert is shown in Figure 150 and is herein designated DNA57836-1338.

The entire nucleotide sequence of DNA57836-1338 is shown in Figure 150 (SEQ ID NO:222). Clone DNA57836-1338 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 63-65 and ending at the stop codon at nucleotide positions 858-860 of SEQ ID NO:222 (Figure 150). The predicted polypeptide precursor is 265 amino acids long (Figure 151). The full-length PRO809 protein shown in Figure 151 has an estimated molecular weight of about 29,061 daltons and a pI of about 9.18. Figure 151 further shows the approximate positions of the signal peptide and N-glycosylation sites. The corresponding nucleotides can be determined by referencing Figure 150. Clone DNA57836-1338 has been deposited with ATCC on June 23, 1998. It is understood that the deposited clone has the actual nucleic acid sequence and that the sequences provided herein are based on known sequencing techniques.

Analysis of the amino acid sequence of the full-length PRO809 polypeptide suggests that it possesses some sequence similarity to the heparin sulfate proteoglycan and to endothelial cell adhesion molecule-1. More specifically, an analysis of the Dayhoff database (version 35.45 SwissProt 35) evidenced sequence identity between the PRO809 amino acid sequence and the following Dayhoff sequences, PGBM\_MOUSE, D82082\_1 and PW14158.

EXAMPLE 65: Isolation of cDNA Clones Encoding Human PRO791

Use of the signal sequence algorithm described in Example 3 above allowed identification of a single Incyte EST cluster sequence. The Incyte EST cluster sequence was then compared to a variety of expressed

sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (LIFESEQ™, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altschul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated DNA56429.

In light of an observed sequence homology between the DNA56429 consensus sequence and an EST sequence encompassed within the Merck EST clone no. 36367, the Merck EST clone 36367 was purchased and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein. The sequence of this cDNA insert is shown in Figure 152 and is herein designated DNA57838-1337.

The entire nucleotide sequence of DNA57838-1337 is shown in Figure 152 (SEQ ID NO:224). Clone DNA57838-1337 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 9-11 and ending at the stop codon at nucleotide positions 747-749 of SEQ ID NO:224 (Figure 152). The predicted polypeptide precursor is 246 amino acids long (Figure 153). The full-length PRO791 protein shown in Figure 153 has an estimated molecular weight of about 27,368 daltons and a pI of about 7.45. Figure 153 also shows the approximate locations of the signal peptide, the transmembrane domain, N-glycosylation sites and a region conserved in extracellular proteins. The corresponding nucleotides of one embodiment provided herein can be identified by referencing Figure 152. Clone DNA57838-1337 has been deposited with ATCC on June 23, 1998. It is understood that the deposited clone has the actual nucleic acid sequence and that the sequences provided herein are based on known sequencing techniques.

Analysis of the amino acid sequence of the full-length PRO791 polypeptide suggests that it has sequence similarity with MHC-I antigens, thereby indicating that PRO791 may be related to MHC-I antigens. More specifically, an analysis of the Dayhoff database (version 35.45 SwissProt 35) evidenced some sequence identity between the PRO791 amino acid sequence and the following Dayhoff sequences, AF034346\_1, MMQ1K5\_1 and HFE\_HUMAN.

#### EXAMPLE 66: Isolation of cDNA clones Encoding Human PRO1004

Use of the signal sequence algorithm described in Example 3 above allowed identification of a single Incyte EST cluster sequence, Incyte cluster sequence No. 73681. This EST cluster sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altschul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, Univ. of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated as DNA56516.

In light of an observed sequence homology between the DNA56516 consensus sequence and an EST sequence encompassed within the Merck EST clone no. H43837, the Merck EST clone H43837 was purchased

and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein. The sequence of this cDNA insert is shown in Figure 154.

The full length clone shown in Figure 154 contained a single open reading frame with an apparent translational initiation site at nucleotide positions 119-121 and ending at the stop codon at nucleotide positions 464-466 (Figure 154; SEQ ID NO:226). The predicted polypeptide precursor is 115 amino acids long (Figure 155; SEQ ID NO:227). The full-length PRO1004 protein shown in Figure 155 has an estimated molecular weight of about 13,649 daltons and a pI of about 9.58. Analysis of the full-length PRO1004 sequence shown in Figure 155 (SEQ ID NO:227) evidences the presence of the following features: a signal peptide at about amino acids 1-24, a microbodies C-terminal targeting signal at about amino acids 113-115, a potential N-glycosylation site at about amino acids 71-74, and a domain having sequence identity with dihydrofolate reductase proteins at about amino acids 22-48.

Analysis of the amino acid sequence of the full-length PRO1004 polypeptide using the Dayhoff database (version 35.45 SwissProt 35) evidenced homology between the PRO1004 amino acid sequence and the following Dayhoff sequences: CELR02D3\_7, LEC1\_MOUSE, AF006691\_3, SSZ97390\_1, SSZ97395\_1, and SSZ97400\_1.

Clone DNA57844-1410 was deposited with the ATCC on June 23, 1998, and is assigned ATCC deposit no. 203010.

#### EXAMPLE 67: Isolation of cDNA clones Encoding Human PRO1111

An expressed sequence tag (EST) DNA database (LIFESEQ®, Incyte Pharmaceuticals, Palo Alto, CA) was searched and an EST was identified which had homology to insulin-like growth factor binding protein.

RNA for construction of cDNA libraries was isolated from human fetal brain. The cDNA libraries used to isolate the cDNA clones encoding human PRO1111 were constructed by standard methods using commercially available reagents such as those from Invitrogen, San Diego, CA. The cDNA was primed with oligo dT containing a NotI site, linked with blunt to SalI hemikinased adaptors, cleaved with NotI, sized appropriately by gel electrophoresis, and cloned in a defined orientation into a suitable cloning vector (such as pRKB or pRKD; pRK5B is a precursor of pRK5D that does not contain the SfiI site; see, Holmes et al., *Science*, 253:1278-1280 (1991)) in the unique XhoI and NotI.

The human fetal brain cDNA libraries (prepared as described above), were screened by hybridization with a synthetic oligonucleotide probe based upon the Incyte EST sequence described above:

5'-CCACCACCTGGAGGTCCTGCAGTTGGGCAGGAAGTCCATCCGGCAGATTG-3' (SEQ ID NO:251).

An identified cDNA clone was sequenced in entirety. The entire nucleotide sequence of PRO1111 is shown in Figure 156 (SEQ ID NO:228). Clone DNA58721-1475 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 57-59 and a stop codon at nucleotide positions 2016-2018 (Figure 156; SEQ ID NO:228). The predicted polypeptide precursor is 653 amino acids long (Figure 157). The transmembrane domains are at positions 21-40 (type II) and 528-548. Clone DNA58721-1475 has been deposited with ATCC and is assigned ATCC deposit no. 203110. The full-length PRO1111 protein shown in Figure 157 has an estimated molecular weight of about 72,717 daltons and a pI of about 6.99.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 157 (SEQ ID NO:229), revealed some sequence identity between the PRO1111 amino acid sequence and the following Dayhoff sequences: A58532, D86983\_1, RNPLGPV\_1, PGS2\_HUMAN, AF038127\_1, ALS\_MOUSE, GPV\_HUMAN, PGS2\_BOVIN, ALS\_PAPPA and I47020.

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**EXAMPLE 68: Isolation of cDNA clones Encoding Human PRO1344**

A consensus DNA sequence was assembled relative to other EST sequences using phrap as described in Example 1 above. This consensus sequence is herein designated DNA33790. Based on the DNA33790 consensus sequence, oligonucleotides were synthesized: 1) to identify by PCR a cDNA library that contained the sequence of interest, and 2) for use as probes to isolate a clone of the full-length coding sequence for PRO1344.

PCR primers (forward and reverse) were synthesized:

forward PCR primer 5'-AGGTTCTGTGATGGAGACAACCGCG-3' (SEQ ID NO:232)

reverse PCR primer 5'-TGTCAGGACGCACTGCCGTCATG-3' (SEQ ID NO:233)

15 Additionally, a synthetic oligonucleotide hybridization probe was constructed from the consensus DNA33790 sequence which had the following nucleotide sequence

hybridization probe

5'-TGGCCAGATCATCAAGCGTGTCTGTGGCAACGAGCGGCCAGCTCCTATCC-3' (SEQ ID NO:234)

20 In order to screen several libraries for a source of a full-length clone, DNA from the libraries was screened by PCR amplification with the PCR primer pair identified above. A positive library was then used to isolate clones encoding the PRO1344 gene using the probe oligonucleotide and one of the PCR primers. RNA for construction of the cDNA libraries was isolated from human fetal kidney tissue.

DNA sequencing of the clones isolated as described above gave the full-length DNA sequence for PRO1344 (designated herein as DNA58723-1588 [Figure 158, SEQ ID NO:230]); and the derived protein sequence for PRO1344.

25 The entire nucleotide sequence of DNA58723-1588 is shown in Figure 158 (SEQ ID NO:230). Clone DNA58723-1588 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 26-28 and ending at the stop codon at nucleotide positions 2186-2188 (Figure 158). The predicted polypeptide precursor is 720 amino acids long (Figure 159). The full-length PRO1344 protein shown in Figure 30 159 has an estimated molecular weight of about 80,199 daltons and a pI of about 7.77. Analysis of the full-length PRO1344 sequence shown in Figure 159 (SEQ ID NO:231) evidences the presence of the following: a signal peptide from about amino acid 1 to about amino acid 23, an EGF-like domain cysteine protein signature sequence from about amino acid 260 to about amino acid 271, potential N-glycosylation sites from about amino acid 96 to about amino acid 99, from about amino acid 279 to about amino acid 282, from about amino acid 316 to about amino acid 319, from about amino acid 451 to about amino acid 454 and from about amino acid 614 to about amino acid 617, an amino acid sequence block having homology to serine proteases, trypsin family from about amino acid 489 to about amino acid 505 and a CUB domain protein profile sequence from about amino

acid 150 to about amino acid 166. Clone DNA58723-1588 has been deposited with ATCC on August 18, 1998 and is assigned ATCC deposit no. 203133.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 159 (SEQ ID NO:231), evidenced significant homology between the PRO1344 amino acid sequence and the following Dayhoff sequences: S77063\_1, CRAR\_MOUSE, P\_R74775, P\_P90070, P\_R09217, P\_P70475, HSBMP16\_1 and U50330\_1.

#### EXAMPLE 69: Isolation of cDNA clones Encoding Human PRO1109

A consensus DNA sequence was assembled relative to other EST sequences using phrap as described in Example 1 above. This consensus sequence is herein designated DNA52642. The consensus DNA sequence was obtained by extending using repeated cycles of BLAST and phrap a previously obtained consensus sequence as far as possible using the sources of EST sequences discussed above. Based on the DNA52642 consensus sequence, oligonucleotides were synthesized: 1) to identify by PCR a cDNA library that contained the sequence of interest, and 2) for use as probes to isolate a clone of the full-length coding sequence for PRO1109.

PCR primers (forward and reverse) were synthesized:

forward PCR primer 5'-CCTTACCTCAGAGGCCAGAGCAAGC-3' (SEQ ID NO:237)

reverse PCR primer 5'-GAGCTTCATCCGTTCTGCGTTCACC-3' (SEQ ID NO:238)

Additionally, a synthetic oligonucleotide hybridization probe was constructed from the consensus DNA52642 sequence which had the following nucleotide sequence

hybridization probe

5'-CAGGAATGTAAAGCTTTACAGAGGGTCGCCATCCTCGTTCCCCACC-3' (SEQ ID NO:239)

In order to screen several libraries for a source of a full-length clone, DNA from the libraries was screened by PCR amplification with the PCR primer pair identified above. A positive library was then used to isolate clones encoding the PRO1109 gene using the probe oligonucleotide and one of the PCR primers. RNA for construction of the cDNA libraries was isolated from human SK-Lu-1 adenocarcinoma cell tissue (LIB247).

DNA sequencing of the clones isolated as described above gave the full-length DNA sequence for PRO1109 (designated herein as DNA58737-1473 [Figure 160, SEQ ID NO:235]) and the derived protein sequence for PRO1109.

The entire nucleotide sequence of DNA58737-1473 is shown in Figure 160 (SEQ ID NO:235). Clone DNA58737-1473 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 119-120 and ending at the stop codon at nucleotide positions 1151-1153 (Figure 160). The predicted polypeptide precursor is 344 amino acids long (Figure 161). The full-length PRO1109 protein shown in Figure 161 has an estimated molecular weight of about 40,041 daltons and a pI of about 9.34. Analysis of the full-length PRO1109 sequence shown in Figure 161 (SEQ ID NO:236) evidences the presence of the following: a signal peptide from about amino acid 1 to about amino acid 27, potential N-glycosylation sites from about amino acid 4 to about amino acid 7, from about amino acid 220 to about amino acid 223 and from about amino acid 335 to about amino acid 338 and an amino acid sequence block having homology to xylose isomerase proteins from about amino acid 191 to about amino acid 201. Clone DNA58737-1473 has been deposited with ATCC

on August 18, 1998 and is assigned ATCC deposit no. 203136.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 161 (SEQ ID NO:236), evidenced significant homology between the PRO1109 amino acid sequence and the following Dayhoff sequences: HSUDPGAL\_1, HSUDPB14\_1, NALS\_BOVIN, HSU10473\_1, CEW02B12\_11, YNJ4\_CAEEL, AE000738\_11, CET24D1\_1,  
 5 S48121 and CEGLY9\_1.

#### EXAMPLE 70: Isolation of cDNA clones Encoding Human PRO1383

A consensus DNA sequence was assembled relative to other EST sequences using phrap as described in Example 1 above. This consensus sequence is herein designated DNA53961. Based on the DNA53961  
 10 consensus sequence, oligonucleotides were synthesized: 1) to identify by PCR a cDNA library that contained the sequence of interest, and 2) for use as probes to isolate a clone of the full-length coding sequence for PRO1383.

PCR primers (forward and reverse) were synthesized:

forward PCR primer 5'-CATTCCTTACCCTGGACCCAGCTCC-3' (SEQ ID NO:242)

15 reverse PCR primer 5'-GAAAGGCCACAGCACATCTGGCAG-3' (SEQ ID NO:243)

Additionally, a synthetic oligonucleotide hybridization probe was constructed from the consensus DNA53961 sequence which had the following nucleotide sequence

hybridization probe

5'-CCACGACCCGAGCAACTTCCTCAAGACCGACTTGTTTCTCTACAGC-3' (SEQ ID NO:244)

20 In order to screen several libraries for a source of a full-length clone, DNA from the libraries was screened by PCR amplification with the PCR primer pair identified above. A positive library was then used to isolate clones encoding the PRO1383 gene using the probe oligonucleotide and one of the PCR primers. RNA for construction of the cDNA libraries was isolated from human fetal brain tissue.

DNA sequencing of the clones isolated as described above gave the full-length DNA sequence for  
 25 PRO1383 (designated herein as DNA58743-1609 [Figure 162, SEQ ID NO: 240]) and the derived protein sequence for PRO1383.

The entire nucleotide sequence of DNA58743-1609 is shown in Figure 162 (SEQ ID NO:240). Clone DNA58743-1609 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 122-124 and ending at the stop codon at nucleotide positions 1391-1393 (Figure 162). The predicted  
 30 polypeptide precursor is 423 amino acids long (Figure 163). The full-length PRO1383 protein shown in Figure 163 has an estimated molecular weight of about 46,989 daltons and a pI of about 6.77. Analysis of the full-length PRO1383 sequence shown in Figure 163 (SEQ ID NO:241) evidences the presence of the following: a signal peptide from about amino acid 1 to about amino acid 24, a transmembrane domain from about amino acid 339 to about amino acid 362, and potential N-glycosylation sites from about amino acid 34 to about amino acid  
 35 37, from about amino acid 58 to about amino acid 61, from about amino acid 142 to about amino acid 145, from about amino acid 197 to about amino acid 200, from about amino acid 300 to about amino acid 303 and from about amino acid 364 to about amino acid 367. Clone DNA58743-1609 has been deposited with ATCC on

August 25, 1998 and is assigned ATCC deposit no. 203154.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 163 (SEQ ID NO:241), evidenced significant homology between the PRO1383 amino acid sequence and the following Dayhoff sequences: NMB\_HUMAN, QNR\_COTJA, P\_W38335, P115\_CHICK, P\_W38164, A45993\_1, MMU70209\_1, D83704\_1 and P\_W39176.

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EXAMPLE 71: Isolation of cDNA Clones Encoding Human PRO1003

Use of the signal sequence algorithm described in Example 3 above allowed identification of a single Incyte EST cluster sequence designated herein as 43055. This sequence was then compared to a variety of EST databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (LIFESEQ™, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altshul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated consen01.

In light of an observed sequence homology between the consensus sequence and an EST sequence encompassed within the Incyte EST clone no. 2849382, the Incyte EST clone 2849382 was purchased and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein. The sequence of this cDNA insert is shown in Figure 164.

The entire nucleotide sequence of DNA58846-1409 is shown in Figure 164 (SEQ ID NO:245). Clone DNA58846-1409 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 41-43 and ending at the stop codon at nucleotide positions 293-295 (Figure 164). The predicted polypeptide precursor is 84 amino acids long (Figure 165). The full-length PRO1003 protein shown in Figure 165 has an estimated molecular weight of about 9,408 daltons and a pI of about 9.28. Analysis of the full-length PRO1003 sequence shown in Figure 165 (SEQ ID NO:246) evidences the presence of a signal peptide at amino acids 1 to about 24, and a cAMP- and cGMP-dependent protein kinase phosphorylation site at about amino acids 58 to about 61. Analysis of the amino acid sequence of the full-length PRO1003 polypeptide using the Dayhoff database (version 35.45 SwissProt 35) evidenced homology between the PRO1003 amino acid sequence and the following Dayhoff sequences: AOPCZA363\_3, SRTX\_ATREN, A48298, MHVJHMS\_1, VGL2\_CVMJH, DHDHTC2\_2, CORT\_RAT, TAL6\_HUMAN, P\_W14123, and DVUFI\_2.

EXAMPLE 72: Isolation of cDNA Clones Encoding Human PRO1108

A consensus DNA sequence was assembled relative to other EST sequences using phrap as described in Example 1 above. This consensus sequence is herein designated DNA53237.

In light of an observed sequence homology between the DNA53237 consensus sequence and an EST sequence encompassed within the Incyte EST clone no. 2379881, the Incyte EST clone 2379881 was purchased and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein.



The sequence of this cDNA insert is shown in Figure 166 and is herein designated DNA58848-1472.

The entire nucleotide sequence of DNA58848-1472 is shown in Figure 166 (SEQ ID NO:247). Clone DNA58848-1472 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 77-79 and ending at the stop codon at nucleotide positions 1445-1447 (Figure 166). The predicted polypeptide precursor is 456 amino acids long (Figure 167). The full-length PRO1108 protein shown in Figure 167 has an estimated molecular weight of about 52,071 daltons and a pI of about 9.46. Analysis of the full-length PRO1108 sequence shown in Figure 167 (SEQ ID NO:248) evidences the presence of the following: type II transmembrane domains from about amino acid 22 to about amino acid 42, from about amino acid 156 to about amino acid 176, from about amino acid 180 to about amino acid 199 and from about amino acid 369 to about amino acid 388, potential N-glycosylation sites from about amino acid 247 to about amino acid 250, from about amino acid 327 to about amino acid 330, from about amino acid 328 to about amino acid 331 and from about amino acid 362 to about amino acid 365 and an amino acid block having homology to ER lumen protein retaining receptor protein from about amino acid 153 to about amino acid 190. Clone DNA58848-1472 has been deposited with ATCC on June 9, 1998 and is assigned ATCC deposit no. 209955.

Analysis of the amino acid sequence of the full-length PRO1108 polypeptide suggests that it possesses significant sequence similarity to the LPAAT protein, thereby indicating that PRO1108 may be a novel LPAAT homolog. More specifically, an analysis of the Dayhoff database (version 35.45 SwissProt 35) evidenced significant homology between the PRO1108 amino acid sequence and the following Dayhoff sequences, AF015811\_1, CER07E3\_2, YL35\_CAEEL, S73863, CEF59F4\_4, P\_W06422, MMU41736\_1, MTV008\_39, P\_R99248 and Y67\_BPT7.

#### EXAMPLE 73: Isolation of cDNA Clones Encoding Human PRO1137

The extracellular domain (ECD) sequences (including the secretion signal, if any) of from about 950 known secreted proteins from the Swiss-Prot public protein database were used to search expressed sequence tag (EST) databases. The EST databases included public EST databases (e.g., GenBank) and a proprietary EST DNA database (LIFESEQ™, Incyte Pharmaceuticals, Palo Alto, CA). The search was performed using the computer program BLAST or BLAST2 (Altschul et al., *Methods in Enzymology* 266:460-480 (1996)) as a comparison of the ECD protein sequences to a 6 frame translation of the EST sequence. Using this procedure, Incyte EST No. 3459449, also referred to herein as "DNA7108", was identified as an EST having a BLAST score of 70 or greater that did not encode a known protein.

A consensus DNA sequence was assembled relative to the DNA7108 sequence and other ESTs using repeated cycles of BLAST and the program "phrap" (Phil Green, Univ. of Washington, Seattle, WA). The consensus sequence obtained therefrom is referred to herein as DNA53952.

In light of an observed sequence homology between the DNA53952 consensus sequence and an EST sequence encompassed within the Incyte EST clone no. 3663102, the Incyte EST clone 3663102 was purchased and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein. The sequence of this cDNA insert is shown in Figure 168.

The entire nucleotide sequence of DNA58849-1494 is shown in Figure 168 (SEQ ID NO:249). Clone DNA58849-1494 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 77-79 and ending at the stop codon at nucleotide positions 797-799 (Figure 168). The predicted polypeptide precursor is 240 amino acids long (Figure 169). The full-length PRO1137 protein shown in Figure 169 has an estimated molecular weight of about 26,064 daltons and a pI of about 8.65. Analysis of the full-length PRO1137 sequence shown in Figure 169 (SEQ ID NO:250) evidences the presence of a signal peptide at about amino acids 1 to 14 and a potential N-glycosylation site at about amino acids 101-105.

Analysis of the amino acid sequence of the full-length PRO1137 polypeptide suggests that it possesses significant sequence similarity to ribosyltransferase thereby indicating that PRO1137 may be a novel member of the ribosyltransferase family of proteins. Analysis of the amino acid sequence of the full-length PRO1137 polypeptide using the Dayhoff database (version 35.45 SwissProt 35) evidenced homology between the PRO1137 amino acid sequence and the following Dayhoff sequences: MMART5\_1, NARG\_MOUSE, GEN11909, GEN13794, GEN14406, MMRNART62\_1, and P\_R41876.

#### EXAMPLE 74: Isolation of cDNA clones Encoding Human PRO1138

Use of the signal sequence algorithm described in Example 3 above allowed identification of a single Incyte EST sequence, Incyte cluster sequence no. 165212. This cluster sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (LIFESEQ™, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altschul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated as DNA54224. The assembly included a proprietary Genentech EST designated herein as DNA49140 (Figure 172; SEQ ID NO:254).

In light of an observed sequence homology between the DNA54224 consensus sequence and an EST sequence encompassed within the Incyte EST clone no. 3836613, the Incyte EST clone 3836613 was purchased and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein. The sequence of this cDNA insert is shown in Figure 170 and is the full-length DNA sequence for PRO1138. Clone DNA58850-1495 was deposited with the ATCC on June 9, 1998, and is assigned ATCC deposit no. 209956.

The entire nucleotide sequence of DNA58850-1495 is shown in Figure 170 (SEQ ID NO:252). Clone DNA58850-1495 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 38-40 and ending at the stop codon at nucleotide positions 1043-1045 (Figure 170). The predicted polypeptide precursor is 335 amino acids long (Figure 171). The full-length PRO1138 protein shown in Figure 171 has an estimated molecular weight of about 37,421 Daltons and a pI of about 6.36. Analysis of the full-length PRO1138 sequence shown in Figure 171 (SEQ ID NO:253) evidences the presence of the following features: a signal peptide at about amino acid 1 to about amino acid 22; a transmembrane domain at about amino

acids 224 to about 250; a leucine zipper pattern at about amino acids 229 to about 250; and potential N-glycosylation sites at about amino acids 98-101, 142-145, 148-151, 172-175, 176-179, 204-207, and 291-295.

Analysis of the amino acid sequence of the full-length PRO1138 polypeptide suggests that it possesses significant sequence similarity to the CD84, thereby indicating that PRO1138 may be a novel member of the Ig superfamily of polypeptides. More particularly, analysis of the amino acid sequence of the full-length PRO1138 polypeptide using the Dayhoff database (version 35.45 SwissProt 35) evidenced homology between the PRO1138 amino acid sequence and the following Dayhoff sequences: HSU82988\_1, HUMLY9\_1, P\_R97631, P\_R97628, P\_R97629, P\_R97630, CD48\_RAT, CD2\_HUMAN, P\_P93996, and HUMBGP\_1.

Clone DNA58850-1495 was deposited with ATCC on June 9, 1998, and is assigned ATCC deposit no. 209956.

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#### EXAMPLE 75: Isolation of cDNA clones Encoding Human PRO1054

Use of the signal sequence algorithm described in Example 3 above allowed identification of an EST cluster sequence from the Incyte database, designated 66212. This EST cluster sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (LIFESEQ®, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altschul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated DNA55722.

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In light of an observed sequence homology between the DNA55722 consensus sequence and an EST sequence encompassed within the Incyte EST clone no. 319751, the Incyte EST clone 319751 was purchased and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein. The sequence of this cDNA insert is shown in Figure 173 and is herein designated as DNA58853-1423.

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Clone DNA58853-1423 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 46-48 and ending at the stop codon at nucleotide positions 586-588 (Figure 173). The predicted polypeptide precursor is 180 amino acids long (Figure 174). The full-length PRO1054 protein shown in Figure 174 has an estimated molecular weight of about 20,638 daltons and a pI of about 5.0. Analysis of the full-length PRO1054 sequence shown in Figure 174 (SEQ ID NO:256) evidences the presence of the following: a signal peptide from about amino acid 1 to about amino acid 18, a leucine zipper pattern from about amino acid 155 to about amino acid 176 and amino acid sequence blocks having homology to lipocalin proteins from about amino acid 27 to about amino acid 38 and from about amino acid 110 to about amino acid 120. Clone DNA58853-1423 has been deposited with ATCC on June 23, 1998 and is assigned ATCC deposit no. 203016.

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An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 174 (SEQ ID NO:256), evidenced significant homology between the PRO1054 amino acid sequence and the following Dayhoff sequences: MUP1\_MOUSE, MUP6\_MOUSE, MUP2\_MOUSE, MUP8\_MOUSE, MUP5\_MOUSE, MUP4\_MOUSE, S10124,

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MUPM\_MOUSE, MUP\_RAT and ECU70823\_1.

**EXAMPLE 76: Isolation of cDNA clones Encoding Human PRO994**

Use of the signal sequence algorithm described in Example 3 above allowed identification of an EST cluster sequence from the Incyte database, designated 157555. This EST cluster sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (LIFESEQ®, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altschul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated DNA55728.

In light of an observed sequence homology between the DNA55728 consensus sequence and an EST sequence encompassed within the Incyte EST clone no. 2860366, the Incyte EST clone 2860366 was purchased and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein. The sequence of this cDNA insert is shown in Figure 175 and is herein designated as DNA58855-1422.

Clone DNA58855-1422 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 31-33 and ending at the stop codon at nucleotide positions 718-720 (Figure 175). The predicted polypeptide precursor is 229 amino acids long (Figure 176). The full-length PRO994 protein shown in Figure 176 has an estimated molecular weight of about 25,109 daltons and a pI of about 6.83. Analysis of the full-length PRO994 sequence shown in Figure 176 (SEQ ID NO:258) evidences the presence of the following: transmembrane domains from about amino acid 10 to about amino acid 31, from about amino acid 50 to about amino acid 72, from about amino acid 87 to about amino acid 110 and from about amino acid 191 to about amino acid 213, potential N-glycosylation sites from about amino acid 80 to about amino acid 83, from about amino acid 132 to about amino acid 135, from about amino acid 148 to about amino acid 151 and from about amino acid 163 to about amino acid 166 and an amino acid block having homology to TNFR/NGFR cysteine-rich region proteins from about amino acid 4 to about amino acid 11. Clone DNA58855-1422 has been deposited with ATCC on June 23, 1998 and is assigned ATCC deposit no. 203018.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 176 (SEQ ID NO:258), evidenced significant homology between the PRO994 amino acid sequence and the following Dayhoff sequences: AF027204\_1, TAL6\_HUMAN, ILT4\_HUMAN, JC6205, MMU57570\_1, S40363, ETU56093\_1, S42858, P\_R66849 and P\_R74751.

**EXAMPLE 77: Isolation of cDNA clones Encoding Human PRO812**

Use of the signal sequence algorithm described in Example 3 above allowed identification of an EST cluster sequence from the Incyte database, designated 170079. This EST cluster sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank)

and a proprietary EST DNA database (Lifeseq®, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altschul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated as DNA55721.

In light of an observed sequence homology between the DNA55721 consensus sequence and an EST sequence encompassed within the Incyte EST clone no. 388964, the Incyte EST clone 388964 was purchased and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein. The sequence of this cDNA insert is shown in Figure 177 and is herein designated as DNA59205-1421.

Clone DNA59205-1421 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 55-57 and ending at the stop codon at nucleotide positions 304-306 (Figure 177). The predicted polypeptide precursor is 83 amino acids long (Figure 178). The full-length PRO812 protein shown in Figure 178 has an estimated molecular weight of about 9,201 daltons and a pI of about 9.3. Analysis of the full-length PRO812 sequence shown in Figure 178 (SEQ ID NO:260) evidences the presence of the following: a signal peptide from about amino acid 1 to about amino acid 15, a cAMP- and cGMP-dependent protein kinase phosphorylation site from about amino acid 73 to about amino acid 76 and protein kinase C phosphorylation sites from about amino acid 70 to about amino acid 72 and from about amino acid 76 to about amino acid 78. Clone DNA59205-1421 has been deposited with ATCC on June 23, 1998 and is assigned ATCC deposit no. 203009.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 178 (SEQ ID NO:260), evidenced significant homology between the PRO812 amino acid sequence and the following Dayhoff sequences: P\_W35802, P\_W35803, PSC1\_RAT, S68231, GEN13917, PSC2\_RAT, CC10\_HUMAN, UTER\_RABBIT, AF008595\_1 and A56413.

#### 25 EXAMPLE 78: Isolation of cDNA clones Encoding Human PRO1069

Use of the signal sequence algorithm described in Example 3 above allowed identification of a single Incyte EST sequence designated herein as 100727. This sequence was then compared to a proprietary EST DNA database (LIFESEQ™, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altschul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, Univ. of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated DNA56001.

In light of an observed sequence homology between the DNA56001 consensus sequence and an EST sequence encompassed within the Incyte EST clone no. 3533881, the Incyte EST clone 3533881 was purchased and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein. The sequence of this cDNA insert is shown in Figure 179 and is the full-length DNA sequence for PRO1069.

Clone DNA59211-1450 was deposited with the ATCC on June 9, 1998, and is assigned ATCC deposit no. 209960.

The entire nucleotide sequence of DNA59211-1450 is shown in Figure 179 (SEQ ID NO:261). Clone DNA59211-1450 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 197-199 and ending at the stop codon at nucleotide positions 464-466. The predicted polypeptide precursor is 89 amino acids long (Figure 180). The full-length PRO1069 protein shown in Figure 180 has an estimated molecular weight of about 9,433 daltons and a pI of about 8.21. Analysis of the full-length PRO1069 sequence shown in Figure 180 (SEQ ID NO:262) evidences the presence of the following features: a signal peptide sequence at amino acid 1 to about 16; a transmembrane domain at about amino acids 36 to about 59; potential N-myristoylation sites at about amino acids 41-46, 45-50, and 84-89; and homology with extracellular proteins SCP/Tpx-1/Ag5/PR-1/Sc7 at about amino acids 54 to about 66.

Analysis of the amino acid sequence of the full-length PRO1069 polypeptide suggests that it possesses significant sequence similarity to CHIF, thereby indicating that PRO1069 may be a member of the CHIF family of polypeptides. More particularly, analysis of the amino acid sequence of the full-length PRO1069 polypeptide using the Dayhoff database (version 35.45 SwissProt 35) evidenced homology between the PRO1069 amino acid sequence and the following Dayhoff sequences: CHIF\_RAT, A55571, PLM\_HUMAN, A40533, ATNG\_BOVIN, RIC\_MOUSE, PETD\_SYNY3, VTB1\_XENLA, A05009, and S75086.

Clone DNA59211-1450 was deposited with the ATCC on June 9, 1998, and is assigned ATCC deposit no. 209960.

#### 20 EXAMPLE 79: Isolation of cDNA Clones Encoding Human PRO1129

Use of the signal sequence algorithm described in Example 3 above allowed identification of a single Incyte EST cluster sequence designated herein as 98833. The Incyte EST cluster sequence no. 98833 sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (LIFESEQ™, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altschul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated DNA56038.

30 In light of an observed sequence homology between the DNA56038 consensus sequence and an EST sequence encompassed within the Incyte EST clone no. 1335241, the Incyte EST clone 1335241 was purchased and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein. The sequence of this cDNA insert is shown in Figure 181 and is herein designated DNA59213-1487.

35 The full length clone shown in Figure 181 contained a single open reading frame with an apparent translational initiation site at nucleotide positions 42-44 and ending at the stop codon found at nucleotide positions 1614-1616 (Figure 181; SEQ ID NO:263). The predicted polypeptide precursor is 524 amino acids long, has a calculated molecular weight of approximately 60,310 daltons and an estimated pI of approximately 7.46.

Analysis of the full-length PRO1129 sequence shown in Figure 182 (SEQ ID NO:264) evidences the presence of the following: type II transmembrane domains from about amino acid 13 to about amino acid 32 and from about amino acid 77 to about amino acid 102, a cytochrome P-450 cysteine heme-iron ligand signature sequence from about amino acid 461 to about amino acid 470 and potential N-glycosylation sites from about amino acid 112 to about amino acid 115 and from about amino acid 168 to about amino acid 171. Clone DNA59213-1487  
 5 has been deposited with the ATCC on June 9, 1998 and is assigned ATCC deposit no. 209959.

Analysis of the amino acid sequence of the full-length PRO1129 polypeptide suggests that it possesses sequence similarity to the cytochrome P-450 family of proteins. More specifically, an analysis of the Dayhoff database (version 35.45 SwissProt 35) evidenced some degree of homology between the PRO1129 amino acid sequence and the following Dayhoff sequences, AC004523\_1, S45702, AF054821\_1 and I53015.

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#### EXAMPLE 80: Isolation of cDNA clones Encoding Human PRO1068

Use of the signal sequence algorithm described in Example 3 above allowed identification of an EST cluster sequence from the LIFESEQ® database, designated Incyte cluster no. 141736. This EST cluster sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (LIFESEQ®, Incyte Pharmaceuticals, Palo Alto, CA) to  
 15 identify existing homologies. One or more of the ESTs was derived from a human mast cell line from a patient with mast cell leukemia. The homology search was performed using the computer program BLAST or BLAST2 (Altschul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a  
 20 consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated DNA56094.

In light of an observed sequence homology between the DNA56094 consensus sequence and an EST sequence encompassed within the Incyte EST clone no. 004974, the Incyte EST clone 004974 was purchased and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein.  
 25 The sequence of this cDNA insert is shown in Figure 183 and is herein designated as DNA59214-1449 (SEQ ID NO:265).

The full length clone shown in Figure 183 contained a single open reading frame with an apparent translational initiation site at nucleotide positions 42-44 and ending at the stop codon found at nucleotide positions 414-416 (Figure 183; SEQ ID NO:265). The predicted polypeptide precursor (Figure 184, SEQ ID NO:266)  
 30 is 124 amino acids long. PRO1068 has a calculated molecular weight of approximately 14,284 daltons and an estimated pI of approximately 8.14. The PRO1068 polypeptide has the following additional features, as indicated in Figure 184: a signal peptide sequence at about amino acids 1-20, a urotensin II signature sequence at about amino acids 118-123, a cell attachment sequence at about amino acids 64-66, and a potential cAMP- and cGMP-dependent protein kinase phosphorylation site at about amino acids 112-115.

35 An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 184 (SEQ ID NO:266), revealed homology between the PRO1068 amino acid sequence and the following Dayhoff sequences: HALBOP\_1, MTV043\_36,

150498, and P\_R78445

Clone DNA59214-1449 was deposited with the ATCC on July 1, 1998 and is assigned ATCC deposit no.203046.

**EXAMPLE 81: Isolation of cDNA clones Encoding Human PRO1066**

5 Use of the signal sequence algorithm described in Example 3 above allowed identification of a single Incyte EST cluster sequence designated herein as 79066. The Incyte EST cluster sequence no. 79066 sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (LIFESEQ™, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or  
10 BLAST2 (Altshul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated DNA56121.

In light of an observed sequence homology between the DNA56121 consensus sequence and an EST  
15 sequence encompassed within the Incyte EST clone no. 1515315, the Incyte EST clone 1515315 was purchased and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein. The sequence of this cDNA insert is shown in Figure 185 and is herein designated DNA59215-1425.

The full length clone shown in Figure 185 contained a single open reading frame with an apparent translational initiation site at nucleotide positions 176-178 and ending at the stop codon found at nucleotide  
20 positions 527-529 (Figure 185; SEQ ID NO:267). The predicted polypeptide precursor is 117 amino acids long, has a calculated molecular weight of approximately 12,911 daltons and an estimated pI of approximately 5.46. Analysis of the full-length PRO1066 sequence shown in Figure 186 (SEQ ID NO:268) evidences the presence of the following: a signal peptide from about amino acid 1 to about amino acid 23, a cAMP- and cGMP-dependent protein kinase phosphorylation site from about amino acid 38 to about amino acid 41 and potential  
25 N-myristoylation sites from about amino acid 5 to about amino acid 10, from about amino acid 63 to about amino acid 68 and from about amino acid 83 to about amino acid 88. Clone UNQ524 (DNA59215-1425) has been deposited with the ATCC on June 9, 1998 and is assigned ATCC deposit no. 209961.

Analysis of the amino acid sequence of the full-length PRO1066 polypeptide suggests that it does not possess significant sequence similarity to any known human protein. However, an analysis of the Dayhoff  
30 database (version 35.45 SwissProt 35) evidenced some degree of homology between the PRO1066 amino acid sequence and the following Dayhoff sequences, MOTI\_HUMAN, AF025667\_1, MTCY19H9\_8 and RABIGKCH\_1.

**EXAMPLE 82: Isolation of cDNA Clones Encoding Human PRO1184**

35 Use of the signal sequence algorithm described in Example 3 on ESTs from an Incyte database allowed identification a candidate sequence designated herein as DNA56375. This sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and



a proprietary EST DNA database (LIFESEQ™, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altschul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated DNA56375.

In light of an observed sequence homology between the DNA56375 consensus sequence and an EST sequence encompassed within the Incyte EST clone no. 1428374, the Incyte EST clone 1428374 was purchased and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein. The sequence of this cDNA insert is shown in Figure 187.

The full length clone shown in Figure 187 contained a single open reading frame with an apparent translational initiation site at nucleotide positions 106-108 and ending at the stop codon found at nucleotide positions 532-534 (Figure 187; SEQ ID NO:269). The predicted polypeptide precursor is 142 amino acids long, has a calculated molecular weight of approximately 15,690 daltons and an estimated pI of approximately 9.64. Analysis of the full-length PRO1184 sequence shown in Figure 188 (SEQ ID NO:270) evidences the presence of a signal peptide at about amino acids 1-38. Clone DNA59220-1514 has been deposited with the ATCC on June 9, 1998. It is understood that the deposited clone has the actual sequences and that representations are presented herein.

Analysis of the amino acid sequence of the full-length PRO1184 polypeptide suggests that it possesses some sequence identity with a protein called TIM from *Drosophila virilis*, designated "DVTIMS02\_1" in the Dayhoff data base, (version 35.45 SwissProt 35). Other Dayhoff database (version 35.45 SwissProt 35) sequences having some degree of sequence identity with PRO1184 include: WIS1\_SCHPO, F002186\_1, ATAC00239124 and MSAIPRP\_1.

#### EXAMPLE 83: Isolation of cDNA clones Encoding Human PRO1360

Use of the signal sequence algorithm described in Example 3 above allowed identification of an EST sequence from an Incyte database, designated DNA10572. This EST sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank, Merck/Wash. U.) and a proprietary EST DNA database (LIFESEQ®, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altschul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated DNA57314.

In light of an observed sequence homology between the DNA57314 consensus sequence and an EST sequence encompassed within the Merck EST clone no. AA406443, the Merck EST clone AA406443 was purchased and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein. The sequence of this cDNA insert is shown in Figure 189 and is herein designated as DNA59488-1603.

The full length clone shown in Figure 189 contained a single open reading frame with an apparent translational initiation site at nucleotide positions 54-56 and ending at the stop codon found at nucleotide positions 909-911 (Figure 189; SEQ ID NO:271). The predicted polypeptide precursor (Figure 190, SEQ ID NO:272) is 285 amino acids long. PRO1360 has a calculated molecular weight of approximately 31,433 daltons and an estimated pI of approximately 7.32. Clone DNA59488-1603 was deposited with the ATCC on August 25, 1998 and is assigned ATCC deposit no. 203157.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 190 (SEQ ID NO:272), revealed sequence identity between the PRO1360 amino acid sequence and the following Dayhoff sequences: UN51\_CAEEL, YD4B\_SCHPO, AF000634\_1, GFO\_ZYMMO, YE1J\_SCHPO, D86566\_1, ZMGFO\_1, S76976, PPSA\_SYNY3, and CEF28B1\_4.

#### EXAMPLE 84: Isolation of cDNA clones Encoding Human PRO1029

Use of the signal sequence algorithm described in Example 3 above allowed identification of an EST cluster sequence from the Incyte database, designated 18763. This EST cluster sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (LIFESEQ®, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altschul et al., *Methods in Enzymology* 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated DNA57854.

In light of an observed sequence homology between the DNA57854 consensus sequence and an EST sequence encompassed within the Merck EST clone no. T98880, the Merck EST clone T98880 was purchased and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein. The sequence of this cDNA insert is shown in Figure 191 and is herein designated as DNA59493-1420.

Clone DNA59493-1420 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 39-41 and ending at the stop codon at nucleotide positions 297-299 (Figure 191). The predicted polypeptide precursor is 86 amino acids long (Figure 192). The full-length PRO1029 protein shown in Figure 192 has an estimated molecular weight of about 9,548 daltons and a pI of about 8.52. Analysis of the full-length PRO1029 sequence shown in Figure 192 (SEQ ID NO:274) evidences the presence of the following: a signal peptide from about amino acid 1 to about amino acid 19, an amino acid block having homology to bacterial rhodopsins retinal binding site protein from about amino acid 50 to about amino acid 61, a prenyl group binding site from about amino acid 83 to about amino acid 86 and a potential N-glycosylation site from about amino acid 45 to about amino acid 48. Clone DNA59493-1420 has been deposited with ATCC on July 1, 1998 and is assigned ATCC deposit no. 203050.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 192 (SEQ ID NO:274), evidenced significant

homology between the PRO1029 amino acid sequence and the following Dayhoff sequences: S66088, AF031815\_1, MM4A6L\_1, PSEIS52a-1, S17699 and P\_R63635.

EXAMPLE 85: Isolation of cDNA clones Encoding Human PRO1139

Use of the signal sequence algorithm described in Example 3 above allowed identification of an EST cluster sequence from the Incyte database, designated 4461. This EST cluster sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (LIFESEQ®, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altschul et al., *Methods in Enzymology* 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated DNA57312.

The DNA57312 consensus sequence included a 172 nucleotides long public EST (T62095, Merck/University of Washington public database). This EST clone, identified herein as a putative protein coding sequence, was purchased from Merck, and sequenced to provide the coding sequence of PRO1139 (Figure 193). As noted before, the deduced amino acid sequence of DNA59497-1496 shows a significant sequence identity with the deduced amino acid sequence of HSOBRGRP\_1. The full-length protein (Figure 194) contains a putative signal peptide between amino acid residues 1 and about 28, and three putative transmembrane domains (approximate amino acid residues 33-52, 71-89, 98-120).

EXAMPLE 86: Isolation of cDNA clones Encoding Human PRO1309

An expressed sequence tag (EST) DNA database (LIFESEQ®, Incyte Pharmaceuticals, Palo Alto, CA) was searched and an EST was identified which showed homology to SLIT.

RNA for construction of cDNA libraries was isolated from human fetal brain tissue. The cDNA libraries used to isolate the cDNA clones encoding human PRO1309 were constructed by standard methods using commercially available reagents such as those from Invitrogen, San Diego, CA. The cDNA was primed with oligo dT containing a NotI site, linked with blunt to SalI hemikinased adaptors, cleaved with NotI, sized appropriately by gel electrophoresis, and cloned in a defined orientation into a suitable cloning vector (such as pRKB or pRKD; pRK5B is a precursor of pRK5D that does not contain the SfiI site; see, Holmes et al., *Science*, 253:1278-1280 (1991)) in the unique XhoI and NotI.

The cDNA libraries (prepared as described above), were screened by hybridization with a synthetic oligonucleotide probe derived from the above described Incyte EST sequence:

5'-TCCGTGCAGGGGACGCCTTTCAGAACTGCGCCGAGTTAAGGAAC-3' (SEQ ID NO:279).

A cDNA clone was isolated and sequenced in entirety. The entire nucleotide sequence of DNA59588-1571 is shown in Figure 195 (SEQ ID NO:277). Clone DNA59588-1571 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 720-722 and a stop codon at nucleotide positions 2286-2288 (Figure 195; SEQ ID NO:277). The predicted polypeptide precursor is 522 amino acids

long. The signal peptide is approximately at 1-34 and the transmembrane domain is at approximately 428-450 of SEQ ID NO:278. Clone DNA59588-1571 has been deposited with ATCC and is assigned ATCC deposit no. 203106. The full-length PRO1309 protein shown in Figure 196 has an estimated molecular weight of about 58,614 daltons and a pI of about 7.42.

- 5 An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 196 (SEQ ID NO:278), revealed sequence identity between the PRO1309 amino acid sequence and the following Dayhoff sequences: AB007876\_1, GPV\_MOUSE, ALS\_RAT, P\_R85889, LUM\_CHICK, AB014462\_1, PGS1\_CANFA, CEM88\_7, A58532 and GEN11209.

EXAMPLE 87: Isolation of cDNA Clones Encoding Human PRO1028

- 10 Use of the signal sequence algorithm described in Example 3 above allowed identification of a certain EST cluster sequence from the Incyte database. This EST cluster sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (LIFESEQ®, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altschul et al., Methods in  
15 Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated DNA59603.

- 20 In light of an observed sequence homology between the DNA59603 sequence and an EST sequence contained within Incyte EST clone no. 1497725, the Incyte EST clone no. 1497725 was purchased and the cDNA insert was obtained and sequenced. It was found that the insert encoded a full-length protein. The sequence of this cDNA insert is shown in Figure 197 and is herein designated as DNA59603-1419.

- The entire nucleotide sequence of DNA59603-1419 is shown in Figure 197 (SEQ ID NO:280). Clone DNA59603-1419 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 21-23 and ending at the stop codon at nucleotide positions 612-614 (Figure 197). The predicted polypeptide precursor is 197 amino acids long (Figure 198). The full-length PRO1028 protein shown in Figure 198 has an estimated molecular weight of about 20,832 daltons and a pI of about 8.74. Clone DNA59603-1419 has been deposited with the ATCC. Regarding the sequence, it is understood that the deposited clone contains the correct sequence, and the sequences provided herein are based on known sequencing techniques.

- 30 Analyzing the amino acid sequence of SEQ ID NO:281, the putative signal peptide is at about amino acids 1-19 of SEQ ID NO:281. An N-glycosylation site is at about amino acids 35-38 of SEQ ID NO:281. A C-type lectin domain is at about amino acids 108-117 of SEQ ID NO:281, indicating that PRO513 may be related to or be a lectin. The corresponding nucleotides of these amino acid sequences or others can be routinely determined given the sequences provided herein.

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**EXAMPLE 88: Isolation of cDNA Clones Encoding Human PRO1027**

Use of the signal sequence algorithm described in Example 3 above allowed identification of a certain EST cluster sequence from the Incyte database. This EST cluster sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (LIFESEQ<sup>®</sup>, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The

5 homology search was performed using the computer program BLAST or BLAST2 (Altschul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated DNA56399.

10 In light of an observed sequence homology between the DNA56399 sequence and an EST sequence contained within Incyte EST clone no. 937605, the Incyte EST clone no. 937605 was purchased and the cDNA insert was obtained and sequenced. It was found that the insert encoded a full-length protein. The sequence of this cDNA insert is shown in Figure 199 and is herein designated as DNA59605-1418.

The entire nucleotide sequence of DNA59605-1418 is shown in Figure 199 (SEQ ID NO:282). Clone

15 DNA59605-1418 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 31-33 and ending at the stop codon at nucleotide positions 262-264 (Figure 199). The predicted polypeptide precursor is 77 amino acids long (Figure 200). The full-length PRO1027 protein shown in Figure 200 has an estimated molecular weight of about 8,772 daltons and a pI of about 9.62. Clone DNA59605-1418 has been deposited with the ATCC. Regarding the sequence, it is understood that the deposited clone contains

20 the correct sequence, and the sequences provided herein are based on known sequencing techniques.

Analyzing the amino acid sequence of SEQ ID NO:283, the putative signal peptide is at about amino acids 1-33 of SEQ ID NO:283. The type II fibronectin collagen-binding domain begins at about amino acid 30 of SEQ ID NO:283. The corresponding nucleotides for these amino acid sequences and others can be routinely determined given the sequences provided herein. PRO1027 may be involved in tissue formation or repair.

25 The following Dayhoff designations appear to have some sequence identity with PRO1027: SFT2\_YEAST; ATM3E9\_2; A69826; YM16\_MARPO; E64896; U60193\_2; MTLRAJ205\_1; MCU60315\_70; SPAS\_SHIFL; and S54213.

**EXAMPLE 89: Isolation of cDNA Clones Encoding Human PRO1107**

30 Use of the signal sequence algorithm described in Example 3 above allowed identification of a certain EST cluster sequence from the Incyte database. This EST cluster sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (LIFESEQ<sup>®</sup>, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The

homology search was performed using the computer program BLAST or BLAST2 (Altschul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence

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obtained therefrom is herein designated DNA56402.

In light of an observed sequence homology between the DNA56402 sequence and an EST sequence contained within Incyte EST clone no. 3203694, the Incyte EST clone no. 3203694 was purchased and the cDNA insert was obtained and sequenced. It was found that the insert encoded a full-length protein. The sequence of this cDNA insert is shown in Figure 201 and is herein designated as DNA59606-1471.

- 5 The entire nucleotide sequence of DNA59606-1471 is shown in Figure 201 (SEQ ID NO:284). Clone DNA59606-1471 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 244-246 and ending at the stop codon at nucleotide positions 1675-1677 of SEQ ID NO:284 (Figure 201). The predicted polypeptide precursor is 477 amino acids long (Figure 202). The full-length PRO1107 protein shown in Figure 202 has an estimated molecular weight of about 54,668 daltons and a pI of about 6.33.
- 10 Clone DNA59606-1471 has been deposited with ATCC on June 9, 1998. It is understood that the deposited clone has the actual nucleic acid sequence and that the sequences provided herein are based on known sequencing techniques.

- Analysis of the amino acid sequence of the full-length PRO1107 polypeptide suggests that it possesses significant sequence similarity to phosphodiesterase I/nucleotide pyrophosphatase, human insulin receptor tyrosine kinase inhibitor, alkaline phosphodiesterase and autotaxin, thereby indicating that PRO1107 may have at least one or all of the activities of these proteins, and that PRO1107 is a novel phosphodiesterase. More specifically, an analysis of the Dayhoff database (version 35.45 SwissProt 35) evidenced sequence identity between the PRO1107 amino acid sequence and at least the following Dayhoff sequences: AF005632\_1, P\_R79148, RNU78787\_1, AF060218\_4, A57080 and HUMATXT\_1.

20

EXAMPLE 90: Isolation of cDNA clones Encoding Human PRO1140

- Use of the signal sequence algorithm described in Example 3 above allowed identification of a single Incyte EST sequence, Incyte cluster sequence No. 135917. This sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary
- 25 EST DNA database (LIFESEQ™, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altschul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, Univ. of Washington, Seattle, Washington). The consensus sequence obtained
- 30 therefrom is herein designated DNA56416.

- In light of an observed sequence homology between DNA56416 and an EST sequence contained within Incyte EST clone no. 3345705, Incyte EST clone no. 3345705 was obtained and its insert sequenced. It was found that the insert encoded a full-length protein. The sequence, designated herein as DNA59607-1497, which is shown in Figure 203, is the full-length DNA sequence for PRO1140. Clone DNA59607-1497 was deposited
- 35 with the ATCC on June 9, 1998, and is assigned ATCC deposit no. 209946.

The entire nucleotide sequence of DNA59607-1497 is shown in Figure 203 (SEQ ID NO:286). Clone DNA59607-1497 contains a single open reading frame with an apparent translational initiation site at nucleotide

positions 210-212 and ending at the stop codon at nucleotide positions 975-977 (Figure 203). The predicted polypeptide precursor is 255 amino acids long (Figure 204). The full-length PRO1140 protein shown in Figure 204 has an estimated molecular weight of about 29,405 daltons and a pI of about 7.64. Analysis of the full-length PRO1140 sequence shown in Figure 204 (SEQ ID NO:287) evidences the presence of three transmembrane domains at about amino acids 101 to 118, 141 to 161 and 172 to 191.

5 Analysis of the amino acid sequence of the full-length PRO1140 polypeptide using the Dayhoff database (version 35.45 SwissProt 35) evidenced homology between the PRO1140 amino acid sequence and the following Dayhoff sequences: AF023602\_1, AF000368\_1, CIN3\_RAT, AF003373\_1, GEN13279, and AF003372\_1.

Clone DNA59607-1497 was deposited with the ATCC on June 9, 1998, and is assigned ATCC deposit no. 209946.

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#### EXAMPLE 91: Isolation of cDNA clones Encoding Human PRO1106

Use of the signal sequence algorithm described in Example 3 above allowed identification of a single Incyte EST sequence. This sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (LIFESEQ™, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using  
 15 the computer program BLAST or BLAST2 (Altschul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, Univ. of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated  
 20 DNA56423.

In light of an observed sequence homology between DNA56423 and an EST sequence contained within Incyte EST clone no. 1711247, Incyte EST clone no. 1711247 was obtained and its insert sequenced. It was found that the insert encoded a full-length protein. The sequence, designated herein as DNA59609-1470, which is shown in Figure 205, is the full-length DNA sequence for PRO1106. Clone DNA59609-1470 was deposited  
 25 with the ATCC on June 9, 1998, and is assigned ATCC deposit no. 209963.

The entire nucleotide sequence of DNA59609-1470 is shown in Figure 205 (SEQ ID NO:288). Clone DNA59609-1470 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 61-63 and ending at the stop codon at nucleotide positions 1468-1470 of SEQ ID NO:288 (Figure 205). The predicted polypeptide precursor is 469 amino acids long (Figure 206). The full-length PRO1106 protein  
 30 shown in Figure 206 has an estimated molecular weight of about 52,689 daltons and a pI of about 8.68. It is understood that the skilled artisan can construct the polypeptide or nucleic acid encoding therefor to exclude any one or more of all of these domains. For example, the transmembrane domain region(s) and/or either of the amino terminal or carboxyl end can be excluded. Clone DNA59609-1470 has been deposited with ATCC on June 9, 1998. It is understood that the deposited clone has the actual nucleic acid sequence and that the  
 35 sequences provided herein are based on known sequencing techniques.

Analysis of the amino acid sequence of the full-length PRO1106 polypeptide suggests that it possesses significant sequence similarity to the peroxisomal ca-dependent solute carrier, thereby indicating that PRO1106

may be a novel transporter. More specifically, an analysis of the Dayhoff database (version 35.45 SwissProt 35) evidenced sequence identity between the PRO1106 amino acid sequence and at least the following Dayhoff sequences, AF004161\_1, IG002N01\_25, GDC\_BOVIN and BT1\_MAIZE.

**EXAMPLE 92: Isolation of cDNA clones Encoding Human PRO1291**

5 Use of the signal sequence algorithm described in Example 3 above allowed identification of an EST cluster sequence from the Incyte database, designated 120480. This EST cluster sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (Lifeseq®, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altschul  
10 et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated DNA56425.

In light of an observed sequence homology between the DNA56425 sequence and an EST sequence  
15 encompassed within the Incyte EST clone no. 2798803, the Incyte EST clone 2798803 was purchased and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein. The sequence of this cDNA insert is shown in Figure 207 and is herein designated as DNA59610-1556.

Clone DNA59610-1556 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 61-63 and ending at the stop codon at nucleotide positions 907-909 (Figure 207). The  
20 predicted polypeptide precursor is 282 amino acids long (Figure 208). The full-length PRO1291 protein shown in Figure 208 has an estimated molecular weight of about 30,878 daltons and a pI of about 5.27. Analysis of the full-length PRO1291 sequence shown in Figure 208 (SEQ ID NO:291) evidences the presence of the following: a signal peptide from about amino acid 1 to about amino acid 28, a transmembrane domain from about amino acid 258 to about amino acid 281 and potential N-glycosylation sites from about amino acid 112 to about  
25 amino acid 115, from about amino acid 160 to about amino acid 163, from about amino acid 190 to about amino acid 193, from about amino acid 196 to about amino acid 199, from about amino acid 205 to about amino acid 208, from about amino acid 216 to about amino acid 219 and from about amino acid 220 to about amino acid 223.. Clone DNA59610-1556 has been deposited with ATCC on June 16, 1998 and is assigned ATCC deposit no. 209990.

30 An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 208 (SEQ ID NO:291), evidenced significant homology between the PRO1291 amino acid sequence and the following Dayhoff sequences: HSU90552\_1, HSU90144\_1, AF033107\_1, HSB73\_1, HSU90142\_1, GGCD80\_1, P\_W34452, MOG\_MOUSE, B39371 and P\_R71360.

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EXAMPLE 93: Isolation of cDNA clones Encoding Human PRO1105

Use of the signal sequence algorithm described in Example 3 above allowed identification of an EST cluster sequence from the Incyte database. This EST cluster sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (Lifeseq®, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altshul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated DNA56430.

In light of an observed sequence homology between the DNA56430 sequence and an EST sequence encompassed within the Incyte EST clone no. 1853047, the Incyte EST clone 1853047 was purchased and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein. The sequence of this cDNA insert is shown in Figure 209 and is herein designated as DNA59612-1466.

The entire nucleotide sequence of DNA59612-1466 is shown in Figure 209 (SEQ ID NO:292). Clone DNA59612-1466 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 28-30 and ending at the stop codon at nucleotide positions 568-570 of SEQ ID NO:292 (Figure 209). The predicted polypeptide precursor is 180 amino acids long (Figure 210). The full-length PRO1105 protein shown in Figure 210 has an estimated molecular weight of about 20,040 daltons and a pI of about 8.35. Clone DNA59612-1466 has been deposited with the ATCC on June 9, 1998. It is understood that the deposited clone has the actual nucleic acid sequence and that the sequences provided herein are based on known sequencing techniques.

Analyzing Figure 210, a signal peptide is at about amino acids 1-19 of SEQ ID NO:293 and transmembrane domains are shown at about amino acids 80-99 and 145-162 of SEQ ID NO:293. It is understood that the skilled artisan could form a polypeptide with all of or any combination or individual selection of these regions. It is also understood that the corresponding nucleic acids can be routinely identified and prepared based on the information provided herein.

EXAMPLE 94: Isolation of cDNA clones Encoding Human PRO511

Use of the signal sequence algorithm described in Example 3 above allowed identification of an EST cluster sequence from the Incyte database. This EST cluster sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (Lifeseq®, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altshul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated DNA56434.

In light of an observed sequence homology between the DNA56434 sequence and an EST sequence encompassed within the Incyte EST clone no. 1227491, the Incyte EST clone 1227491 was purchased and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein. The sequence of this cDNA insert is shown in Figure 211 and is herein designated as DNA59613-1417.

The entire nucleotide sequence of DNA59613-1417 is shown in Figure 211 (SEQ ID NO:294). Clone  
 5 DNA59613-1417 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 233-235 and ending at the stop codon at nucleotide positions 944-946 (Figure 211). The predicted polypeptide precursor is 237 amino acids long (Figure 212). The full-length PRO511 protein shown in Figure 212 has an estimated molecular weight of about 25,284 daltons and a pI of about 5.74. Clone DNA59613-1417 has been deposited with the ATCC. Regarding the sequence, it is understood that the deposited clone contains  
 10 the correct sequence, and the sequences provided herein are based on known sequencing techniques.

Analyzing the amino acid sequence of SEQ ID NO:295, the putative signal peptide is at about amino acids 1-25 of SEQ ID NO:295. The N-glycosylation sites are at about amino acids 45-48, 73-76, 107-110, 118-121, 132-135, 172-175, 175-178 and 185-188 of SEQ ID NO:295. An arthropod defensins conserved region is at about amino acids 176-182 of SEQ ID NO:295. A kringle domain begins at about amino acid 128 of SEQ  
 15 ID NO:295 and a ly-6/u-PAR domain begins at about amino acid 6 of SEQ ID NO:295. The corresponding nucleotides of these amino acid sequences and others can be routinely determined given the sequences provided herein.

The designations appearing in a Dayhoff database with which PRO511 has some sequence identity are as follows: SSC20F10\_1; SF041083; P\_W26579; S44208; JC2394; PSTA\_DICDI; A27020; S59310;  
 20 RAG1\_RABIT; and MUSBALBC1\_1.

#### EXAMPLE 95: Isolation of cDNA clones Encoding Human PRO1104

Use of the signal sequence algorithm described in Example 3 above allowed identification of an EST cluster sequence from the Incyte database. This EST cluster sequence was then compared to a variety of  
 25 expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (Lifeseq®, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altschul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with  
 30 the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated DNA56446.

In light of an observed sequence homology between the DNA56446 sequence and an EST sequence encompassed within the Incyte EST clone no. 2837496, the Incyte EST clone 2837496 was purchased and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein. The  
 35 sequence of this cDNA insert is shown in Figure 213 and is herein designated as DNA59616-1465.

The entire nucleotide sequence of DNA59616-1465 is shown in Figure 213 (SEQ ID NO:296). Clone DNA59616-1465 contains a single open reading frame with an apparent translational initiation site at nucleotide

positions 109-111 and ending at the stop codon at nucleotide positions 1132-1134 of SEQ ID NO:296 (Figure 213). The predicted polypeptide precursor is 341 amino acids long (Figure 214). The full-length PRO1104 protein shown in Figure 214 has an estimated molecular weight of about 36,769 daltons and a pI of about 9.03. Clone DNA59616-1465 has been deposited with ATCC on June 16, 1998. It is understood that the deposited clone has the actual nucleic acid sequence and that the sequences provided herein are based on known sequencing techniques.

Analyzing Figure 214, a signal peptide is at about amino acids 1-22 of SEQ ID NO:297. N-myristoylation sites are at about amino acids 41-46, 110-115, 133-138, 167-172 and 179-184 of SEQ ID NO:297.

#### 10 EXAMPLE 96: Isolation of cDNA clones Encoding Human PRO1100

Use of the signal sequence algorithm described in Example 3 above allowed identification of an EST cluster sequence from the Incyte database. This EST cluster sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (Lifeseq®, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altschul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington).

In light of an observed sequence homology between the obtained consensus sequence and an EST sequence encompassed within the Incyte EST clone no. 2305379, the Incyte EST clone 2305379 was purchased and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein. The sequence of this cDNA insert is shown in Figure 215 and is herein designated as DNA59619-1464.

The entire nucleotide sequence of DNA59619-1464 is shown in Figure 215 (SEQ ID NO:298). Clone DNA59619-1464 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 33-35 and ending at the stop codon at nucleotide positions 993-995 of SEQ ID NO:298 (Figure 215). The predicted polypeptide precursor is 320 amino acids long (Figure 216). The full-length PRO1100 protein shown in Figure 216 has an estimated molecular weight of about 36,475 daltons and a pI of about 7.29. Clone DNA59619-1464 has been deposited with ATCC on July 1, 1998. It is understood that the deposited clone has the actual nucleic acid sequence and that the sequences provided herein are based on known sequencing techniques.

Upon analyzing SEQ ID NO:299, the approximate locations of the signal peptide, the transmembrane domains, an N-glycosylation site, an N-myristoylation site, a CUB domain and an amiloride-sensitive sodium channel domain are present. It is believed that PRO1100 may function as a channel. The corresponding nucleic acids for these amino acids and others can be routinely determined given SEQ ID NO:299..

**EXAMPLE 97: Isolation of cDNA clones Encoding Human PRO836**

Use of the signal sequence algorithm described in Example 3 above allowed identification of an EST cluster sequence from the Incyte database. This EST cluster sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (Lifeseq®, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The  
5 homology search was performed using the computer program BLAST or BLAST2 (Altschul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained is herein designated DNA56453.

10 In light of an observed sequence homology between the DNA56453 consensus sequence and an EST sequence encompassed within the Incyte EST clone no. 2610075, the Incyte EST clone 2610075 was purchased and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein. The sequence of this cDNA insert is shown in Figure 217 and is herein designated as DNA59620-1463.

The entire nucleotide sequence of DNA59620-1463 is shown in Figure 217 (SEQ ID NO:300). Clone  
15 DNA59620-1463 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 65-67 and ending at the stop codon at nucleotide positions 1448-1450 of SEQ ID NO:300 (Figure 217). The predicted polypeptide precursor is 461 amino acids long (Figure 218). The full-length PRO836 protein shown in Figure 218 has an estimated molecular weight of about 52,085 daltons and a pI of about 5.36. Analysis of the full-length PRO836 sequence shown in Figure 218 (SEQ ID NO:301) evidences the presence of the  
20 following: a signal peptide, N-glycosylation sites, N-myristoylation sites, a domain conserved in the YJL126w/YLR351c/yhcX family of proteins, and a region having sequence identity with SLS1. Clone DNA59620-1463 has been deposited with ATCC on June 16, 1998. It is understood that the deposited clone has the actual nucleic acid sequence and that the sequences provided herein are based on known sequencing techniques.

25 Analysis of the amino acid sequence of the full-length PRO836 polypeptide suggests that it possesses some sequence similarity to SLS1, thereby indicating that PRO836 may be involved in protein translocation of the ER. More specifically, an analysis of the Dayhoff database (version 35.45 SwissProt 35) evidenced some homology between the PRO836 amino acid sequence and at least the following Dayhoff sequences, S58132, SPBC3B9\_1, S66714, CRU40057\_1 and IMA\_CAEEL.

30

**EXAMPLE 98: Isolation of cDNA clones Encoding Human PRO1141**

Use of the signal sequence algorithm described in Example 3 above allowed identification of an EST cluster sequence from the Incyte database, designated 11873. This EST cluster sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank)  
35 and a proprietary EST DNA database (LIFESEQ®, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altschul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or

in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated DNA56518.

In light of an observed sequence homology between the DNA56518 consensus sequence and an EST sequence encompassed within the Incyte EST clone no. 2679995, the Incyte EST clone 2679995 was purchased and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein. The sequence of this cDNA insert is shown in Figure 219 and is herein designated as DNA59625-1498.

Clone DNA59625-1498 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 204-206 and ending at the stop codon at nucleotide positions 945-947 (Figure 219). The predicted polypeptide precursor is 247 amino acids long (Figure 220). The full-length PRO1141 protein shown in Figure 220 has an estimated molecular weight of about 26,840 daltons and a pI of about 8.19. Analysis of the full-length PRO1141 sequence shown in Figure 220 (SEQ ID NO:303) evidences the presence of the following: a signal peptide from about amino acid 1 to about amino acid 19 and transmembrane domains from about amino acid 38 to about amino acid 57, from about amino acid 67 to about amino acid 83, from about amino acid 117 to about amino acid 139 and from about amino acid 153 to about amino acid 170. Clone DNA59625-1498 has been deposited with ATCC on June 16, 1998 and is assigned ATCC deposit no. 209992.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 220 (SEQ ID NO:303), evidenced significant homology between the PRO1141 amino acid sequence and the following Dayhoff sequences: CEVF36H2L\_2, PCRB7PRJ\_1, AB000506\_1, LEU95008\_1, MRU87980\_15, YIGM\_ECOLI, STU65700\_1, GHU62778\_1, CYST\_SYNY3 and AF009567\_1.

#### EXAMPLE 99: Isolation of cDNA clones Encoding Human PRO1132

A consensus DNA sequence was assembled relative to other EST sequences using phrap as described in Example 1 above. This consensus sequence is designated herein as DNA35934. Based on the DNA35934 consensus sequence, oligonucleotides were synthesized: 1) to identify by PCR a cDNA library that contained the sequence of interest, and 2) for use as probes to isolate a clone of the full-length coding sequence for PRO1132.

PCR primers (forward and reverse) were synthesized:

forward PCR primer: 5'-TCCTGTGACCACCCCTCTAACACC-3' (SEQ ID NO:310) and  
reverse PCR primer: 5'-CTGGAACATCTGCTGCCAGATTC-3' (SEQ ID NO:311).

Additionally, a synthetic oligonucleotide hybridization probe was constructed from the consensus sequence which had the following nucleotide sequence:

5'-GTCGGATGACAGCAGCAGCCGCATCATCAATGGATCCGACTGCGATATGC-3' (SEQ ID NO:312).

In order to screen several libraries for a source of a full-length clone, DNA from the libraries was screened by PCR amplification with the PCR primer pair identified above. A positive library was then used to isolate clones encoding the PRO1132 gene using the probe oligonucleotide and one of the PCR primers. RNA for construction of the cDNA libraries was isolated from human fetal kidney.

DNA sequencing of the clones isolated as described above gave the full-length DNA sequence for PRO1132 and the derived protein sequence for PRO1132.

The entire nucleotide sequence of PRO1132 is shown in Figure 225 (SEQ ID NO:308). Clone DNA59767-1489 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 354-356 and a stop codon at nucleotide positions 1233-1235 (Figure 225; SEQ ID NO:308). The predicted polypeptide precursor is 293 amino acids long. The signal peptide is at about amino acids 1-22 and the histidine active site is at about amino acids 104-109 of SEQ ID NO:309. Clone DNA59767-1489 has been deposited with ATCC (having the actual sequence rather than representations based on sequencing techniques as presented herein) and is assigned ATCC deposit no. 203108. The full-length PRO1132 protein shown in Figure 226 has an estimated molecular weight of about 32,020 daltons and a pI of about 8.7.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 226 (SEQ ID NO:309), revealed sequence identity between the PRO1132 amino acid sequence and the following Dayhoff sequences: SSU76256\_1, P\_W10694, MMAE000663\_6, AF013988\_1, U66061\_8, MMAE000665\_2, MMAE00066415, MMAE00066414, MMAE000665\_4 and MMAE00066412.

#### EXAMPLE 100: Isolation of cDNA clones Encoding Human NL7 (PRO1346)

A single EST sequence (#1398422) was found in the LIFESEQ<sup>®</sup> database as described in Example 1 above. This EST sequence was renamed as DNA45668. Based on the DNA45668 sequence, oligonucleotides were synthesized: 1) to identify by PCR a cDNA library that contained the sequence of interest, and 2) for use as probes to isolate a clone of the full-length coding sequence for NL7.

PCR primers (forward and reverse) were synthesized:

forward PCR primer: 5'-CACACGTCCAACCTCAATGGGCAG-3' (SEQ ID NO:315)

reverse PCR primer: 5'-GACCAGCAGGGCCAAGGACAAGG-3' (SEQ ID NO:316)

Additionally, a synthetic oligonucleotide hybridization probe was constructed from the consensus DNA45668 sequence which had the following nucleotide sequence:

hybridization probe:

5'-GTTCTCTGAGATGAAGATCCGGCCGGTCCGGGAGTACCGCTTAG-3'

(SEQ ID NO:317)

In order to screen several libraries for a source of a full-length clone, DNA from the libraries was screened by PCR amplification with the PCR primer pair identified above. A positive library was then used to isolate clones encoding the NL7 gene using the probe oligonucleotide and one of the PCR primers. RNA for construction of the cDNA libraries was isolated from a human fetal kidney library (LIB227).

DNA sequencing of the clones isolated as described above gave the full-length DNA sequence for NL7 (designated herein as DNA59776-1600 [Figure 227, SEQ ID NO:313]) and the derived protein sequence for NL7 (PRO1346).

The entire coding sequence of NL7 (PRO1346) is shown in Figure 227 (SEQ ID NO:313). Clone DNA59776-1600 contains a single open reading frame with an apparent translational initiation site at nucleotide

positions 1-3 and an apparent stop codon at nucleotide positions 1384-1386. The predicted polypeptide precursor is 461 amino acids long. The protein contains an apparent type II transmembrane domain at amino acid positions from about 31 to about 50; fibrinogen beta and gamma chains C-terminal domain signature starting at about amino acid position 409, and a leucine zipper pattern starting at about amino acid positions 140, 147, 154 and 161, respectively. Clone DNA59776-1600 has been deposited with ATCC and is assigned ATCC deposit no. 203128. The full-length NL7 protein shown in Figure 228 has an estimated molecular weight of about 50,744 daltons and a pI of about 6.38.

Based on a WU-BLAST2 sequence alignment analysis (using the WU-BLAST2 computer program) of the full-length sequence, NL7 shows significant amino acid sequence identity to a human microfibril-associated glycoprotein (1 MFA4\_HUMAN); to known TIE-2 ligands and ligand homologues, ficolin, serum lectin and TGF-1 binding protein.

#### EXAMPLE 101: Isolation of cDNA clones Encoding Human PRO1131

A cDNA sequence isolated in the amylase screen described in Example 2 above is herein designated DNA43546 (see Figure 231; SEQ ID NO:320). The DNA43546 sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (LIFESEQ™, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altschul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into consensus DNA sequences with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated DNA45627.

Based on the DNA45627 sequence, oligonucleotide probes were generated and used to screen a human library prepared as described in paragraph 1 of Example 2 above. The cloning vector was pRK5B (pRK5B is a precursor of pRK5D that does not contain the SfiI site; see, Holmes et al., Science 253:1278-1280 (1991)), and the cDNA size cut was less than 2800 bp.

PCR primers (forward and 2 reverse) were synthesized:

forward PCR primer 5'-ATGCAGGCCAAGTACAGCAGCAC-3' (SEQ ID NO:321);

reverse PCR primer 1 5'-CATGCTGACGACTTCCTGCAAGC-3' (SEQ ID NO:322); and

reverse PCR primer 1 5'-CCACACAGTCTCTGCTTCTTGGG-3' (SEQ ID NO:323)

Additionally, a synthetic oligonucleotide hybridization probe was constructed from the DNA45627 sequence which had the following nucleotide sequence:

hybridization probe

5'-ATGCTGGATGATGATGGGGACACCACCATGAGCCTGCATT-3' (SEQ ID NO:324).

In order to screen several libraries for a source of a full-length clone, DNA from the libraries was screened by PCR amplification with the PCR primer pair identified above. A positive library was then used to isolate clones encoding the PRO1131 gene using the probe oligonucleotide and one of the PCR primers.

A full length clone was identified that contained a single open reading frame with an apparent translational initiation site at nucleotide positions 144-146, and a stop signal at nucleotide positions 984-986 (Figure 229; SEQ ID NO:318). The predicted polypeptide precursor is 280 amino acids long, has a calculated molecular weight of approximately 31,966 daltons and an estimated pI of approximately 6.26. The transmembrane domain sequence is at about 49-74 of SEQ ID NO:319 and the region having sequence identity with LDL receptors is about 50-265 of SEQ ID NO:319. PRO1131 contains potential N-linked glycosylation sites at amino acid positions 95-98 and 169-172 of SEQ ID NO:319. Clone DNA59777-1480 has been deposited with the ATCC and is assigned ATCC deposit no. 203111.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 230 (SEQ ID NO:319), evidenced some sequence identity between the PRO1131 amino acid sequence and the following Dayhoff sequences: AB010710\_1, I49053, I49115, RNU56863\_1, LY4A\_MOUSE, I55686, MMU56404\_1, I49361, AF030313\_1 and MMU09739\_1.

#### EXAMPLE 102: Isolation of cDNA clones Encoding Human PRO1281

A consensus DNA sequence was assembled relative to other EST sequences using phrap as described in Example 1 above. This consensus sequence is designated herein as DNA35720. Based on the DNA35720 sequence, oligonucleotides were synthesized: 1) to identify by PCR a cDNA library that contained the sequence of interest, and 2) for use as probes to isolate a clone of the full-length coding sequence for PRO1281.

PCR primers (forward and reverse) were synthesized:

#### forward PCR primers:

- 20 5'-TGGAAGGCTGCCGCAACGACAATC-3' (SEQ ID NO:327);  
5'-CTGATGTGGCCGATGTTCTG-3' (SEQ ID NO:328); and  
5'-ATGGCTCAGTGTGCAGACAG-3' (SEQ ID NO:329).

#### reverse PCR primers:

- 5'-GCATGCTGCTCCGTGAAGTAGTCC-3' (SEQ ID NO:330); and  
25 5'-ATGCATGGGAAAGAAGGCCTGCCC-3' (SEQ ID NO:331).

Additionally, a synthetic oligonucleotide hybridization probe was constructed from the DNA35720 sequence which had the following nucleotide sequence:

#### hybridization probe:

- 5'-TGCACTGGTGACCACGAGGGGGTGCACTATAGCCATCTGGAGCTGAG-3' (SEQ ID NO:332).  
30 In order to screen several libraries for a source of a full-length clone, DNA from the libraries was screened by PCR amplification with the PCR primer pairs identified above. A positive library was then used to isolate clones encoding the PRO1281 gene using the probe oligonucleotide and one of the PCR primers. RNA for construction of the cDNA libraries was isolated human fetal liver.

DNA sequencing of the clones isolated as described above gave the full-length DNA sequence for PRO1281 (designated herein as DNA59820-1549 [Figure 232, SEQ ID NO:325]; and the derived protein sequence for PRO1281.



The entire coding sequence of PRO1281 is shown in Figure 232 (SEQ ID NO:325). Clone DNA59820-1549 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 228-230 and an apparent stop codon at nucleotide positions 2553-2555. The predicted polypeptide precursor is 775 amino acids long. The full-length PRO1281 protein shown in Figure 233 has an estimated molecular weight of about 85,481 daltons and a pI of about 6.92. Additional features include a signal peptide at about amino acids 1-15; and potential N-glycosylation sites at about amino acids 138-141 and 361-364.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 233 (SEQ ID NO:326), revealed some sequence identity between the PRO1281 amino acid sequence and the following Dayhoff sequences: S44860, CET24D1\_1, CEC38H2\_3, CAC2\_HAECO, B3A2\_HUMAN, S22373, CEF38A3\_2, CEC34F6\_2, CEC34F6\_3, and CELT22B11\_3.

Clone DNA59820-1549 has been deposited with ATCC and is assigned ATCC deposit no. 203129.

#### EXAMPLE 103: Isolation of cDNA clones Encoding Human PRO1064

A cDNA sequence isolated in the amylase screen described in Example 2 above was found, by the WU-BLAST2 sequence alignment computer program, to have no significant sequence identity to any known human protein. This cDNA sequence is herein designated DNA45288. The DNA45288 sequence was then compared to various EST databases including public EST databases (e.g., GenBank), and a proprietary EST database (LIFESEQ®, Incyte Pharmaceuticals, Palo Alto, CA) to identify homologous EST sequences. The comparison was performed using the computer program BLAST or BLAST2 [Altschul et al., Methods in Enzymology, 266:460-480 (1996)]. Those comparisons resulting in a BLAST score of 70 (or in some cases, 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). This consensus sequence is herein designated DNA48609. Oligonucleotide primers based upon the DNA48609 sequence were then synthesized and employed to screen a human fetal kidney cDNA library which resulted in the identification of the DNA59827-1426 clone shown in Figure 234. The cloning vector was pRK5B (pRK5B is a precursor of pRK5D that does not contain the SfiI site; see, Holmes et al., Science, 253:1278-1280 (1991)), and the cDNA size cut was less than 2800 bp.

The oligonucleotide probes employed were as follows:

forward PCR primer 5'-CTGAGACCCTGCAGCACCATCTG-3' (SEQ ID NO:336)

reverse PCR primer 5'-GGTGCTTCTTGAGCCCCACTTAGC-3' (SEQ ID NO:337)

Additionally, a synthetic oligonucleotide hybridization probe was constructed from the consensus DNA48609 sequence which had the following nucleotide sequence

hybridization probe

5'-AATCTAGCTTCTCCAGGACTGTGGTCGCCCCGTCGCTGT-3' (SEQ ID NO:338)

A full length clone was identified that contained a single open reading frame with an apparent translational initiation site at nucleotide positions 532-534 and a stop signal at nucleotide positions 991-993 (Figure 234, SEQ ID NO:333). The predicted polypeptide precursor is 153 amino acids long, has a calculated

molecular weight of approximately 17,317 daltons and an estimated pI of approximately 5.17. Analysis of the full-length PRO1064 sequence shown in Figure 235 (SEQ ID NO:334) evidences the presence of the following: a signal peptide from about amino acid 1 to about amino acid 24, a transmembrane domain from about amino acid 89 to about amino acid 110, an indole-3-glycerol phosphate synthase homology block from about amino acid 74 to about amino acid 105 and a Myb DNA binding domain protein repeat protein homology block from about amino acid 114 to about amino acid 137. Clone DNA59827-1426 has been deposited with ATCC on August 4, 1998 and is assigned ATCC deposit no. 203089.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 235 (SEQ ID NO:334), evidenced homology between the PRO1064 amino acid sequence and the following Dayhoff sequences: MMNP15PRO\_1, BP187PLYH\_1, CELF42G8\_4, MMU58888\_1, GEN14270, TUB8\_SOLTU, RCN\_MOUSE, HUMRBSY79\_1, SESENODA\_1 and A21467\_1.

#### EXAMPLE 104: Isolation of cDNA clones Encoding Human PRO1379

A consensus DNA sequence was assembled relative to other EST sequences using phrap as described in Example 1 above. This consensus sequence is designated herein DNA45232. Based on the DNA45232 consensus sequence, oligonucleotides were synthesized: 1) to identify by PCR a cDNA library that contained the sequence of interest, and 2) for use as probes to isolate a clone of the full-length coding sequence for PRO1379.

PCR primers (forward and reverse) were synthesized:

forward PCR primer 5'-TGGACACCGTACCCTGGTATCTGC-3' (SEQ ID NO:341)  
reverse PCR primer 5'-CCAACTCTGAGGAGAGCAAGTGGC-3' (SEQ ID NO:342)

Additionally, a synthetic oligonucleotide hybridization probe was constructed from the consensus DNA45232 sequence which had the following nucleotide sequence:

hybridization probe  
 5'-TGTATGTGCACACCCTCACCATCACCTCCAAGGGCAAGGAGAAC-3' (SEQ ID NO:343).

In order to screen several libraries for a source of a full-length clone, DNA from the libraries was screened by PCR amplification with the PCR primer pair identified above. A positive library was then used to isolate clones encoding the PRO1379 gene using the probe oligonucleotide and one of the PCR primers. RNA for construction of the cDNA libraries was isolated human fetal kidney tissue.

DNA sequencing of the clones isolated as described above gave the full-length DNA sequence for PRO1379 which is designated herein as DNA59828-1608 and shown in Figure 237 (SEQ ID NO:339); and the derived protein sequence for PRO1379 (SEQ ID NO:340).

The entire coding sequence of PRO1379 is shown in Figure 237 (SEQ ID NO:339). Clone DNA59828-1608 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 10-12 and an apparent stop codon at nucleotide positions 1732-1734. The predicted polypeptide precursor is 574 amino acids long. The full-length PRO1379 protein shown in Figure 238 has an estimated molecular weight of about 65,355 daltons and a pI of about 8.73. Additional features include a signal peptide at about amino acids

1-17 and potential N-glycosylation sites at about amino acids 160-163, 287-290, and 323-326.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 238 (SEQ ID NO:340), revealed some homology between the PRO1379 amino acid sequence and the following Dayhoff sequences: YHY8\_YEAST, AF040625\_1, HP714394\_1, and HIV18U45630\_1.

- 5           Clone DNA59828-1608 has been deposited with ATCC and is assigned ATCC deposit no. 203158.

EXAMPLE 105: Isolation of cDNA Clones Encoding Human PRO844

- An expressed sequence tag (EST) DNA database (LIFESEQ™, Incyte Pharmaceuticals, Palo Alto, CA) was searched and an EST was identified which showed sequence identity with aLP. Based on the information and discoveries provided herein, the clone for this EST, Incyte clone no. 2657496 from a cancerous lung library was further examined.
- 10

DNA sequencing of the insert for this clone gave a sequence (herein designated as DNA59838-1462; SEQ ID NO:344) which includes the full-length DNA sequence for PRO844 and the derived protein sequence for PRO844.

- 15           The entire nucleotide sequence of DNA59838-1462 is shown in Figure 239 (SEQ ID NO:344). Clone DNA59838-1462 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 5-7 and ending at the stop codon at nucleotide positions 338-340 of SEQ ID NO:344 (Figure 239). The predicted polypeptide precursor is 111 amino acids long (Figure 240). The full-length PRO844 protein shown in Figure 240 has an estimated molecular weight of about 12,050 daltons and a pI of about 5.45. Clone
- 20           UNQ544 DNA59838-1462 has been deposited with ATCC on June 16, 1998. It is understood that the deposited clone has the actual nucleic acid sequence and that the sequences provided herein are based on known sequencing techniques.

- Analysis of the amino acid sequence of the full-length PRO844 polypeptide suggests that it possesses significant sequence similarity to serine protease inhibitors, thereby indicating that PRO844 may be a novel
- 25           proteinase inhibitor. More specifically, an analysis of the Dayhoff database (version 35.45 SwissProt 35) evidenced significant homology between the PRO844 amino acid sequence and at least the following Dayhoff sequences, ALK1\_HUMAN, P\_P82403, P\_P82402, ELAF\_HUMAN and P\_P60950.

EXAMPLE 106: Isolation of cDNA Clones Encoding Human PRO848

- 30           Use of the signal sequence algorithm described in Example 3 above allowed identification of a single EST cluster sequence from the Incyte database. This EST cluster sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (LIFESEQ®, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altschul et al., Methods in
- 35           Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence

obtained therefrom is herein designated DNA55999.

In light of an observed sequence homology between the DNA55999 consensus sequence and an EST sequence encompassed within the Incyte EST clone no. 2768571, the Incyte EST clone 2768571 was purchased and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein. The sequence of this cDNA insert is shown in Figure 241 and is herein designated as DNA59839-1461.

5 The entire nucleotide sequence of DNA59839-1461 is shown in Figure 241 (SEQ ID NO:346). Clone DNA59839-1461 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 146-148 and ending at the stop codon at nucleotide positions 1946-1948 of SEQ ID NO:346 (Figure 241). The predicted polypeptide precursor is 600 amino acids long (Figure 242). The full-length PRO848 protein shown in Figure 242 has an estimated molecular weight of about 68,536 daltons. Clone DNA59839-1461  
10 has been deposited with ATCC on June 16, 1998. It is understood that the deposited clone has the actual nucleic acid sequence and that the sequences provided herein are based on known sequencing techniques.

Analysis of the amino acid sequence of the full-length PRO848 polypeptide suggests that it may be a novel sialyltransferase. More specifically, an analysis of the Dayhoff database (version 35.45 SwissProt 35) evidenced sequence identity between the PRO848 amino acid sequence and at least the following Dayhoff  
15 sequences, P\_R78619 (GalNAc-alpha-2, 6-sialyltransferase), CAAG5\_CHICK (alpha-n-acetylgalactosamide alpha-2, 6-sialyltransferase), HSU14550\_1, CAG6\_HUMAN and P\_R63217 (human alpha-2, 3-sialyltransferase).

#### EXAMPLE 107: Isolation of cDNA Clones Encoding Human PRO1097

Use of the signal sequence algorithm described in Example 3 above allowed identification of a single  
20 EST cluster sequence from the Incyte database. This EST cluster sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (LIFESEQ®, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altschul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90)  
25 or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated DNA56006.

In light of an observed sequence homology between the DNA56006 consensus sequence and an EST sequence encompassed within the Incyte EST clone no. 2408105, the Incyte EST clone 2408105 was purchased  
30 and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein. The sequence of this cDNA insert is shown in Figure 243 and is herein designated as DNA59841-1460.

The entire nucleotide sequence of DNA59841-1460 is shown in Figure 243 (SEQ ID NO:348). Clone DNA59841-1460 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 3-5 and ending at the stop codon at nucleotide positions 276-278 of SEQ ID NO:348 (Figure 243).  
35 The predicted polypeptide precursor is 91 amino acids long (Figure 244). The full-length PRO1097 protein shown in Figure 244 has an estimated molecular weight of about 10,542 daltons and a pI of about 10.04. Clone DNA59841-1460 has been deposited with ATCC on July 1, 1998. It is understood that the deposited clone has

the actual nucleic acid sequence and that the sequences provided herein are based on known sequencing techniques.

Analyzing Figure 244, the signal peptide is at about amino acids 1-20 of SEQ ID NO:349. The glycoprotease family protein domain starts at about amino acid 56, and the acyltransferase ChoActase/COT/CPT family peptide starts at about amino acid 49 of SEQ ID NO:349.

5

#### EXAMPLE 108: Isolation of cDNA clones Encoding Human PRO1153

Use of the signal sequence algorithm described in Example 3 above allowed identification of a single EST cluster sequence from the Incyte database. This EST cluster sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (LIFESEQ®, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altschul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated DNA56008.

In light of an observed sequence homology between the DNA56008 consensus sequence and an EST sequence encompassed within the Incyte EST clone no. 2472409, the Incyte EST clone 2472409 was purchased and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein. The sequence of this cDNA insert is shown in Figure 245 and is herein designated as DNA59842-1502.

The full length clone shown in Figure 245 contained a single open reading frame with an apparent translational initiation site at nucleotide positions 92-94 and ending at the stop codon found at nucleotide positions 683-685 (Figure 245; SEQ ID NO:350). The predicted polypeptide precursor (Figure 246, SEQ ID NO:351) is 197 amino acids long. PRO1153 has a calculated molecular weight of approximately 21,540 daltons and an estimated pI of approximately 8.31. Clone DNA59842-1502 has been deposited with ATCC and is assigned ATCC deposit no. 209982. It is understood that the correct and actual sequence is in the deposited clone while herein are present representations based on current sequencing techniques which may have minor errors.

Based on a WU-BLAST2 sequence alignment analysis (using the ALIGN computer program) of the full-length sequence, PRO1153 shows some amino acid sequence identity to the following Dayhoff designations: S57447; SOYHRGPC\_1; S46965; P\_P82971; VCPHEROPH\_1; EXTN\_TOBAC; MLCB2548\_9; ANXA\_RABIT; JC5437 and SSGP\_VOLCA.

#### EXAMPLE 109: Isolation of cDNA clones Encoding Human PRO1154

Use of the signal sequence algorithm described in Example 3 above allowed identification of a single EST cluster sequence from the Incyte database. This EST cluster sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (LIFESEQ®, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altschul et al., Methods in

Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated DNA56025.

In light of an observed sequence homology between the DNA56025 consensus sequence and an EST sequence encompassed within the Incyte EST clone no. 2169375, the Incyte EST clone 2169375 was purchased and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein. The sequence of this cDNA insert is shown in Figure 247 and is herein designated as DNA59846-1503.

The full length clone shown in Figure 247 contained a single open reading frame with an apparent translational initiation site at nucleotide positions 86-88 and ending at the stop codon found at nucleotide positions 2909-2911 (Figure 247; SEQ ID NO:352). The predicted polypeptide precursor (Figure 248, SEQ ID NO:353) is 941 amino acids long. PRO1154 has a calculated molecular weight of approximately 107,144 daltons and an estimated pI of approximately 6.26. Clone DNA59846-1503 has been deposited with ATCC and is assigned ATCC deposit no. 209978.

Based on a WU-BLAST2 sequence alignment analysis (using the ALIGN computer program) of the full-length sequence, PRO1154 shows sequence identity to at least the following Dayhoff designations: AB011097\_1, AMPN\_HUMAN, RNU76997\_1, 159331, GEN14047, HSU62768\_1, P\_R51281, CET07F10\_1, SSU66371\_1, and AMPRE\_HUMAN.

#### EXAMPLE 110: Isolation of cDNA clones Encoding Human PRO1181

Use of the signal sequence algorithm described in Example 3 above allowed identification of a single EST cluster sequence from the Incyte database, designated herein as 82468. This EST cluster sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (LIFESEQ®, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altschul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated DNA56029.

In light of an observed sequence homology between the DNA56029 consensus sequence and an EST sequence encompassed within the Incyte EST clone no. 2186536, the Incyte EST clone 2186536 was purchased and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein. The sequence of this cDNA insert is shown in Figure 249 and is herein designated as DNA59847-1511.

Clone DNA59847-1511 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 17-19 and ending at the stop codon at nucleotide positions 1328-1330 (Figure 249). The predicted polypeptide precursor is 437 amino acids long (Figure 250). The full-length PRO1181 protein shown in Figure 250 has an estimated molecular weight of about 46,363 daltons and a pI of about 6.22. Analysis of the full-length PRO1181 sequence shown in Figure 250 (SEQ ID NO:355) evidences the presence of the

following: a signal peptide from about amino acid 1 to about amino acid 15, potential N-glycosylation sites from about amino acid 46 to about amino acid 49, from about amino acid 189 to about amino acid 192 and from about amino acid 382 to about amino acid 385 and amino acid sequence blocks having homology to Ly-6/u-PAR domain proteins from about amino acid 287 to about amino acid 300 and from about amino acid 98 to about amino acid 111. Clone DNA59847-1511 has been deposited with ATCC on August 4, 1998 and is assigned  
 5 ATCC deposit no. 203098.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 250 (SEQ ID NO:355), evidenced homology between the PRO1181 amino acid sequence and the following Dayhoff sequences: AF041083\_1, P\_W26579, RNMAPIAN\_1, CELT13C2\_2, LMSAP2GN\_1, S61882, CEF35C5\_12, DP87\_DICDI, GIU47631\_1 and  
 10 P\_R07092.

#### EXAMPLE 111: Isolation of cDNA clones Encoding Human PRO1182

Use of the signal sequence algorithm described in Example 3 above allowed identification of a single EST cluster sequence from the Incyte database, designated herein as 146647. This EST cluster sequence was  
 15 then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (LIFESEQ®, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altschul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and  
 20 assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated DNA56033.

In light of an observed sequence homology between the DNA56033 consensus sequence and an EST sequence encompassed within the Incyte EST clone no. 2595195, the Incyte EST clone 2595195 was purchased and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein.  
 25 The sequence of this cDNA insert is shown in Figure 251 and is herein designated as DNA59848-1512.

Clone DNA59848-1512 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 67-69 and ending at the stop codon at nucleotide positions 880-882 (Figure 251). The predicted polypeptide precursor is 271 amino acids long (Figure 252). The full-length PRO1182 protein shown in Figure 252 has an estimated molecular weight of about 28,665 daltons and a pI of about 5.33. Analysis of  
 30 the full-length PRO1182 sequence shown in Figure 252 (SEQ ID NO:357) evidences the presence of the following: a signal peptide from about amino acid 1 to about amino acid 25, an amino acid block having homology to C-type lectin domain proteins from about amino acid 247 to about amino acid 256 and an amino acid sequence block having homology to C1q domain proteins from about amino acid 44 to about amino acid 77. Clone DNA59848-1512 has been deposited with ATCC on August 4, 1998 and is assigned ATCC deposit  
 35 no. 203088.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 252 (SEQ ID NO:357), evidenced significant

homology between the PRO1182 amino acid sequence and the following Dayhoff sequences: PSPD\_BOVIN, CL43\_BOVIN, CONG\_BOVIN, P\_W18780, P\_R45005, P\_R53257 and CELEGAP7\_1.

**EXAMPLE 112: Isolation of cDNA clones Encoding Human PRO1155**

Use of the signal sequence algorithm described in Example 3 above allowed identification of a single  
 5 EST cluster sequence from the Incyte database. This EST cluster sequence was then compared to a variety of  
 expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary  
 EST DNA database (LIFESEQ®, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The  
 homology search was performed using the computer program BLAST or BLAST2 (Altschul et al., Methods in  
Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90)  
 10 or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with  
 the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence  
 obtained therefrom is herein designated DNA56102.

In light of an observed sequence homology between the DNA56102 consensus sequence and an EST  
 sequence encompassed within the Incyte EST clone no. 2858870, the Incyte EST clone 2858870 was purchased  
 15 and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein.  
 The sequence of this cDNA insert is shown in Figure 253 and is herein designated as DNA59849-1504.

The full length clone shown in Figure 253 contained a single open reading frame with an apparent  
 translational initiation site at nucleotide positions 158-160 and ending at the stop codon found at nucleotide  
 positions 563-565 (Figure 253; SEQ ID NO:358). The predicted polypeptide precursor (Figure 254, SEQ ID  
 20 NO:359) is 135 amino acids long. PRO1155 has a calculated molecular weight of approximately 14,833 daltons  
 and an estimated pI of approximately 9.78. Clone DNA59849-1504 has been deposited with ATCC and is  
 assigned ATCC deposit no. 209986. It is understood that the actual clone has the correct sequence whereas  
 herein are only representations which are prone to minor sequencing errors.

Based on a WU-BLAST2 sequence alignment analysis (using the ALIGN computer program) of the full-  
 25 length sequence, PRO1155 shows some amino acid sequence identity with the following Dayhoff designations:  
 TKNK\_BOVIN; PVB19X587\_1; AF019049\_1; P\_W00948; S72864; P\_W00949; I62742; AF038501\_1;  
 TKNG\_HUMAN; and YAT1\_RHOBL. Based on the information provided herein, PRO1155 may play a role  
 in providing neuroprotection and cognitive enhancement.

**EXAMPLE 113: Isolation of cDNA clones Encoding Human PRO1156**

Use of the signal sequence algorithm described in Example 3 above allowed identification of a single  
 EST cluster sequence from the Incyte database, designated herein as 138851. This EST cluster sequence was  
 then compared to a variety of expressed sequence tag (EST) databases which included public EST databases  
 (e.g., GenBank) and a proprietary EST DNA database (LIFESEQ®, Incyte Pharmaceuticals, Palo Alto, CA) to  
 35 identify existing homologies. The homology search was performed using the computer program BLAST or  
 BLAST2 (Altschul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a  
 BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and



assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated DNA56261.

In light of an observed sequence homology between the DNA56261 consensus sequence and an EST sequence encompassed within the Incyte EST clone no. 3675191, the Incyte EST clone 3675191 was purchased and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein.

- 5 The sequence of this cDNA insert is shown in Figure 255 and is herein designated as DNA59853-1505.

The full length clone shown in Figure 255 contained a single open reading frame with an apparent translational initiation site at nucleotide positions 212-214 and ending at the stop codon found at nucleotide positions 689-691 (Figure 255; SEQ ID NO:360). The predicted polypeptide precursor (Figure 256, SEQ ID NO:361) is 159 amino acids long. PRO1156 has a calculated molecular weight of approximately 17,476 daltons, 10 an estimated pI of approximately 9.15, a signal peptide sequence at about amino acids 1 to about 22, and potential N-glycosylation sites at about amino acids 27-30 and 41-44.

Clone DNA59853-1505 was deposited with the ATCC on June 16, 1998 and is assigned ATCC deposit no. 209985.

- 15 An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis (using the ALIGN computer program) of the full-length sequence shown in Figure 256 (SEQ ID NO:361), revealed some homology between the PRO1156 amino acid sequence and the following Dayhoff sequences: D45027\_1, P\_R79914, JC5309, KBF2\_HUMAN, AF010144\_1, GEN14351, S68681, P\_R79915, ZMTAC\_3, and HUMCPGO\_1.

20 EXAMPLE 114: Isolation of cDNA Clones Encoding Human PRO1098

- Use of the signal sequence algorithm described in Example 3 above allowed identification of a single EST cluster sequence from the Incyte database. This EST cluster sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (LIFESEQ<sup>®</sup>, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The 25 homology search was performed using the computer program BLAST or BLAST2 (Altschul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated DNA56377.

- 30 In light of an observed sequence homology between the DNA56377 consensus sequence and an EST sequence encompassed within the Incyte EST clone no. 3050917, the Incyte EST clone 3050917 was purchased and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein. The sequence of this cDNA insert is shown in Figure 257 and is herein designated as DNA59854-1459.

- The entire nucleotide sequence of DNA59854-1459 is shown in Figure 257 (SEQ ID NO:362). Clone 35 DNA59854-1459 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 58-60 and ending at the stop codon at nucleotide positions 292-294 of SEQ ID NO:362 (Figure 257). The predicted polypeptide precursor is 78 amino acids long (Figure 258). The full-length PRO1098 protein

shown in Figure 258 has an estimated molecular weight of about 8,396 daltons and a pI of about 7.66. Clone DNA59854-1459 has been deposited with ATCC on June 16, 1998. It is understood that the deposited clone has the actual nucleic acid sequence and that the sequences provided herein are based on known sequencing techniques.

- 5 Analyzing Figure 258, a signal peptide appears to be at about amino acids 1-19 of SEQ ID NO:363. an N-glycosylation site appears to be at about amino acids 37-40 of SEQ ID NO:363, and N-myristoylation sites appear to be at about 15-20, 19-24 and 60-65 of SEQ ID NO:363.

**EXAMPLE 115: Isolation of cDNA clones Encoding Human PRO1127**

- 10 Use of the signal sequence algorithm described in Example 3 above allowed identification of a single EST cluster sequence from the Incyte database. This EST cluster sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (LIFESEQ®, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altschul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated DNA57959.

- 15 In light of an observed sequence homology between the DNA57959 consensus sequence and an EST sequence encompassed within the Merck EST clone no. 685126, the Merck EST clone 685126 was purchased and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein. The sequence of this cDNA insert is shown in Figure 259 and is herein designated as DNA60283-1484.

- 20 The full length clone shown in Figure 259 contained a single open reading frame with an apparent translational initiation site at nucleotide positions 126-128 and ending at the stop codon found at nucleotide positions 327-329 (Figure 259; SEQ ID NO:364). The predicted polypeptide precursor (Figure 260, SEQ ID NO:365) is 67 amino acids long including a signal peptide at about 1-29 of SEQ ID NO:365. PRO1127 has a calculated molecular weight of approximately 7,528 daltons and an estimated pI of approximately 4.95. Clone DNA60283-1484 was deposited with the ATCC on July 1, 1998 and is assigned ATCC deposit no. 203043. It is understood that the deposited clone has the actual sequence, whereas representations which may have minor sequencing errors are presented herein.

- 30 An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 260 (SEQ ID NO:365), revealed some homology between the PRO1127 amino acid sequence and the following Dayhoff sequences: AF037218\_48, P\_W09638, HBA\_HETPO, S39821, KR2\_EBV, CET20D3\_8, HCU37630\_1, HS193B12\_10, S40012 and TRITUBC\_1.

35

**EXAMPLE 116: Isolation of cDNA clones Encoding Human PRO1126**

Use of the signal sequence algorithm described in Example 3 above allowed identification of a single EST cluster sequence from the Incyte database. This EST cluster sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (LIFESEQ®, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altschul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated DNA56250.

- 10 In light of an observed sequence homology between the DNA56250 consensus sequence and an EST sequence encompassed within the Incyte EST clone no. 1437250, the Incyte EST clone 1437250 was purchased and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein. The sequence of this cDNA insert is shown in Figure 261 and is herein designated as DNA60615-1483.

- 15 Clone DNA60615-1483 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 110-112 and ending at the stop codon at nucleotide positions 1316-1318 (Figure 261). The predicted polypeptide precursor is 402 amino acids long (Figure 262). The full-length PRO1126 protein shown in Figure 262 has an estimated molecular weight of about 45,921 daltons and a pI of about 8.60. Analysis of the full-length PRO1126 sequence shown in Figure 262 (SEQ ID NO:367) evidences the presence of the following: a signal peptide from about amino acid 1 to about amino acid 25 and potential N-glycosylation sites from about amino acid 66 to about amino acid 69, from about amino acid 138 to about amino acid 141 and from about amino acid 183 to about amino acid 186. Clone DNA60615-1483 has been deposited with ATCC on June 16, 1998 and is assigned ATCC deposit no. 209980.

- 20 An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 262 (SEQ ID NO:367), evidenced significant homology between the PRO1126 amino acid sequence and the following Dayhoff sequences: I73636, NOMR\_HUMAN, MMUSMYOC3\_1, HS454G6\_1, P\_R98225, RNU78105\_1, RNU72487\_1, AF035301\_1, CEELC48E7\_4 and CEF11C3\_3.

**EXAMPLE 117: Isolation of cDNA clones Encoding Human PRO1125**

- 30 Use of the signal sequence algorithm described in Example 3 above allowed identification of a single EST cluster sequence from the Incyte database. This EST cluster sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (LIFESEQ®, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altschul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence

obtained therefrom is herein designated DNA56540.

In light of an observed sequence homology between the DNA56540 consensus sequence and an EST sequence encompassed within the Incyte EST clone no. 1486114, the Incyte EST clone 1486114 was purchased and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein. The sequence of this cDNA insert is shown in Figure 263 and is herein designated as DNA60615-1483.

- 5 The full length clone shown in Figure 263 contained a single open reading frame with an apparent translational initiation site at nucleotide positions 47-49 and ending at the stop codon found at nucleotide positions 1388-1390 (Figure 263; SEQ ID NO:368). The predicted polypeptide precursor (Figure 264, SEQ ID NO:369) is 447 amino acids long. PRO1125 has a calculated molecular weight of approximately 49,798 daltons and an estimated pI of approximately 9.78. Clone DNA60619-1482 has been deposited with ATCC and is assigned  
 10 ATCC deposit no. 209993. It is understood that the clone has the actual sequence and that the sequences herein are representations based on current techniques which may be prone to minor errors.

- Based on a WU-BLAST2 sequence alignment analysis (using the ALIGN computer program) of the full-length sequence, PRO1125 shows some sequence identity with the following Dayhoff designations: RCO1\_NEUCR; S58306; PKWA\_THECU; S76086; P\_R85881; HET1\_PODAN; SPU92792\_1;  
 15 APAF\_HUMAN; S76414 and S59317.

#### EXAMPLE 118: Isolation of cDNA clones Encoding Human PRO1186

- Use of the signal sequence algorithm described in Example 3 above allowed identification of a single EST cluster sequence from the Incyte database. This EST cluster sequence was then compared to a variety of  
 20 expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (LIFESEQ®, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altschul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with  
 25 the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated DNA56748.

- In light of an observed sequence homology between the DNA56748 consensus sequence and an EST sequence encompassed within the Incyte EST clone no. 3476792, the Incyte EST clone 3476792 was purchased and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein.  
 30 The sequence of this cDNA insert is shown in Figure 265 and is herein designated as DNA60621-1516.

- The full length clone shown in Figure 265 contained a single open reading frame with an apparent translational initiation site at nucleotide positions 91-93 and ending at the stop codon found at nucleotide positions 406-408 (Figure 265; SEQ ID NO:370). The predicted polypeptide precursor (Figure 266, SEQ ID NO:371) is 105 amino acids long. The signal peptide is at amino acids 1-19 of SEQ ID NO:371. PRO1186 has a  
 35 calculated molecular weight of approximately 11,715 daltons and an estimated pI of approximately 9.05. Clone DNA60621-1516 was deposited with the ATCC on August 4, 1998 and is assigned ATCC deposit no. 203091.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 266 (SEQ ID NO:371), revealed some sequence identity between the PRO1186 amino acid sequence and the following Dayhoff sequences: VPRA\_DENPO, LFE4\_CHICK, AF034208\_1, AF030433\_1, A55035, COL\_RABIT, CELB0507\_9, S67826\_1, S34665 and CRU73817\_1.

5

EXAMPLE 119: Isolation of cDNA clones Encoding Human PRO1198

An initial DNA sequence referred to herein as DNA52083 was identified using a yeast screen in a human umbilical vein endothelial cell cDNA library that preferentially represents the 5' ends of the primary cDNA clones. DNA52083 was compared to ESTs from public databases (e.g., GenBank), and a proprietary  
10 EST database (LIFESEQ®, Incyte Pharmaceuticals, Palo Alto, CA), using the computer program BLAST or BLAST2 [Altschul et al., Methods in Enzymology, 266:460-480 (1996)]. The ESTs were clustered and assembled into a consensus DNA sequence using the computer program "phrap" (Phil Green, University of Washington, Seattle, Washington). One or more of the ESTs was obtained from human breast skin tissue biopsy. This consensus sequence is designated herein as DNA52780.

15 In light of an observed sequence homology between the DNA52780 consensus sequence and an EST sequence encompassed within the Incyte EST clone no. 3852910, the Incyte EST clone 3852910 was purchased and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein. The sequence of this cDNA insert is shown in Figure 267 and is herein designated as DNA60622-1525.

The full length DNA60622-1525 clone shown in Figure 267 (SEQ ID NO:372) contained a single open  
20 reading frame with an apparent translational initiation site at nucleotide positions 54 to 56 and ending at the stop codon found at nucleotide positions 741 to 743. The predicted polypeptide precursor, which is shown in Figure 268 (SEQ ID NO:373), is 229 amino acids long. PRO1198 has a calculated molecular weight of approximately 25,764 daltons and an estimated pI of approximately 9.17. There is a signal peptide sequence at about amino acids 1 through 34. There is sequence identity with glycosyl hydrolases family 31 protein at about amino acids  
25 142 to about 175.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 268 (SEQ ID NO:373), revealed some homology between the PRO1198 amino acid sequence and the following Dayhoff sequences: ATF6H11\_6, UCRI\_RAT, TOBSUP2NT\_1, RCUERF3\_1, AMU88186\_1, P\_W22485, S56579, AF040711\_1, DPP4\_PIG.

30 Clone DNA60622-1525 has been deposited with the ATCC on August 4, 1998, and is assigned ATCC deposit no. 203090.

EXAMPLE 120: Isolation of cDNA clones Encoding Human PRO1158

Use of the signal sequence algorithm described in Example 3 above allowed identification of a single  
35 EST cluster sequence from the Incyte database. This EST cluster sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (LIFESEQ®, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The

homology search was performed using the computer program BLAST or BLAST2 (Altschul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated DNA57248.

- 5 In light of an observed sequence homology between the DNA57248 consensus sequence and an EST sequence encompassed within the Incyte EST clone no. 2640776, the Incyte EST clone 2640776 was purchased and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein. The sequence of this cDNA insert is shown in Figure 269 and is herein designated as DNA60625-1507.

- 10 The full length clone shown in Figure 269 contained a single open reading frame with an apparent translational initiation site at nucleotide positions 163 to 165 and ending at the stop codon found at nucleotide positions 532 to 534 (Figure 269; SEQ ID NO:374). The predicted polypeptide precursor (Figure 270, SEQ ID NO:375) is 123 amino acids long. PRO1158 has a calculated molecular weight of approximately 13,113 daltons and an estimated pI of approximately 8.53. Additional features include a signal peptide sequence at about amino acids 1-19, a transmembrane domain at about amino acids 56-80, and a potential N-glycosylation site at  
15 about amino acids 36-39. Clone DNA60625-1507 was deposited with the ATCC on June 16, 1998 and is assigned ATCC deposit no. 209975.

- An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 270 (SEQ ID NO:375), revealed some homology between the PRO1158 amino acid sequence and the following Dayhoff sequences: ATAC00310510F18A8.10,  
20 P\_R85151, PHS2\_SOLTU, RNMHCIBAC\_1, RNA1FMHC\_1, I68771, RNRT1A10G\_1, PTPA\_HUMAN, HUMGACA\_1, and CHKPTPA\_1.

#### EXAMPLE 121: Isolation of cDNA clones Encoding Human PRO1159

- Use of the signal sequence algorithm described in Example 3 above allowed identification of a single  
25 EST cluster sequence from the Incyte database. This EST cluster sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (LIFESEQ®, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altschul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90)  
30 or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated DNA57221.

- In light of an observed sequence homology between the DNA57221 consensus sequence and an EST sequence encompassed within the Incyte EST clone no. 376776, the Incyte EST clone 376776 was purchased  
35 and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein. The sequence of this cDNA insert is shown in Figure 271 and is herein designated as DNA60627-1508.

Clone DNA60627-1508 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 92-94 and ending at the stop codon at nucleotide positions 362-364 (Figure 271). The predicted polypeptide precursor is 90 amino acids long (Figure 272). The full-length PRO1159 protein shown in Figure 272 has an estimated molecular weight of about 9,840 daltons and a pI of about 10.13. Analysis of the full-length PRO1159 sequence shown in Figure 272 (SEQ ID NO:377) evidences the presence of the following: a signal peptide from about amino acid 1 to about amino acid 15 and a potential N-glycosylation site from about amino acid 38 to about amino acid 41. Clone DNA60627-1508 has been deposited with ATCC on August 4, 1998 and is assigned ATCC deposit no. 203092.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 272 (SEQ ID NO:377), evidenced significant homology between the PRO1159 amino acid sequence and the following Dayhoff sequences: AF016494\_6, AF036708\_20, DSSCUTE\_1, D89100\_1, S28060, MEFA\_XENLA, AF020798\_12, G70065, E64423, JQ2005.

#### EXAMPLE 122: Isolation of cDNA clones Encoding Human PRO1124

Use of the signal sequence algorithm described in Example 3 above allowed identification of a single EST cluster sequence from the Incyte database. This EST cluster sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (LIFESEQ®, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altschul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated DNA56035.

In light of an observed sequence homology between the DNA56035 consensus sequence and an EST sequence encompassed within the Incyte EST clone no. 2767646, the Incyte EST clone 2767646 was purchased and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein. The sequence of this cDNA insert is shown in Figure 273 and is herein designated as DNA60629-1481.

The full length clone shown in Figure 273 contained a single open reading frame with an apparent translational initiation site at nucleotide positions 25-27 and ending at the stop codon found at nucleotide positions 2782-2784 (Figure 273; SEQ ID NO:378). The predicted polypeptide precursor (Figure 274, SEQ ID NO:379) is 919 amino acids long. PRO1124 has a calculated molecular weight of approximately 101,282 daltons and an estimated pI of approximately 5.37. Clone DNA60629-1481 has been deposited with the ATCC and is assigned ATCC deposit no. 209979. It is understood that the deposited clone has the actual sequence, whereas only representations based on current sequencing techniques which may include normal and minor errors, are provided herein.

Based on a WU-BLAST2 sequence alignment analysis of the full-length sequence, PRO1124 shows significant amino acid sequence identity to a chloride channel protein and to ECAM-1. Specifically, the following Dayhoff designations were identified as having sequence identity with PRO1124: ECLC\_BOVIN,

AF001261\_1, P\_W06548, SSC6A10\_1, AF004355\_1, S76691, AF017642, BYU06866\_2, CSA\_DICDI and SAU47139\_2.

**EXAMPLE 123: Isolation of cDNA clones Encoding Human PRO1287**

An expressed sequence tag (EST) DNA database (LIFESEQ®, Incyte Pharmaceuticals, Palo Alto, CA) was searched and an EST was identified which showed homology to the fringe protein. This EST sequence was then compared to various EST databases including public EST databases (e.g., GenBank), and a proprietary EST database (LIFESEQ®, Incyte Pharmaceuticals, Palo Alto, CA) to identify homologous EST sequences. The comparison was performed using the computer program BLAST or BLAST2 [Altschul et al., Methods in Enzymology, 266:460-480 (1996)]. Those comparisons resulting in a BLAST score of 70 (or in some cases, 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). This consensus sequence obtained is herein designated DNA40568.

Based on the DNA40568 consensus sequence, oligonucleotides were synthesized: 1) to identify by PCR a cDNA library that contained the sequence of interest, and 2) for use as probes to isolate a clone of the full-length coding sequence for PRO1287. Forward and reverse PCR primers generally range from 20 to 30 nucleotides and are often designed to give a PCR product of about 100-1000 bp in length. The probe sequences are typically 40-55 bp in length. In some cases, additional oligonucleotides are synthesized when the consensus sequence is greater than about 1-1.5kbp. In order to screen several libraries for a full-length clone, DNA from the libraries was screened by PCR amplification, as per Ausubel et al., Current Protocols in Molecular Biology, *supra*, with the PCR primer pair. A positive library was then used to isolate clones encoding the gene of interest using the probe oligonucleotide and one of the primer pairs.

PCR primers (forward and reverse) were synthesized:

forward PCR primer 5'-CTCGGGGAAAGGGACTTGATGTTGG-3' (SEQ ID NO:382)

reverse PCR primer 1 5'-GCGAAGGTGAGCCTCTATCTCGTGCC-3' (SEQ ID NO:383)

25 reverse PCR primer 2 5'-CAGCCTACACGTATTGAGG-3' (SEQ ID NO:384)

Additionally, a synthetic oligonucleotide hybridization probe was constructed from the consensus DNA40568 sequence which had the following nucleotide sequence

hybridization probe

5'-CAGTCAGTACAATCCTGGCATAATATACGGCCACCATGATGCAGTCCC-3' (SEQ ID NO:385).

30 In order to screen several libraries for a source of a full-length clone, DNA from the libraries was screened by PCR amplification with the PCR primer pairs identified above. A positive library was then used to isolate clones encoding the PRO1287 gene using the probe oligonucleotide and one of the PCR primers.

RNA for construction of the cDNA libraries was isolated from human bone marrow tissue. The cDNA libraries used to isolated the cDNA clones were constructed by standard methods using commercially available reagents such as those from Invitrogen, San Diego, CA. The cDNA was primed with oligo dT containing a NotI site, linked with blunt to SalI hemikinased adaptors, cleaved with NotI, sized appropriately by gel electrophoresis, and cloned in a defined orientation into a suitable cloning vector (such as pRKB or pRKD;



pRK5B is a precursor of pRK5D that does not contain the SfiI site; see, Holmes et al., *Science*, 253:1278-1280 (1991)) in the unique XhoI and NotI sites.

DNA sequencing of the clones isolated as described above gave the full-length DNA sequence for PRO1287 (designated herein as DNA61755-1554 [Figure 275, SEQ ID NO:380]) and the derived protein sequence for PRO1287.

- 5 The entire nucleotide sequence of DNA61755-1554 is shown in Figure 275 (SEQ ID NO:380). The full length clone contained a single open reading frame with an apparent translational initiation site at nucleotide positions 655-657 and a stop signal at nucleotide positions 2251-2253 (Figure 275, SEQ ID NO:380). The predicted polypeptide precursor is 532 amino acids long, has a calculated molecular weight of approximately 61,351 daltons and an estimated pI of approximately 8.77. Analysis of the full-length PRO1287 sequence shown  
10 in Figure 276 (SEQ ID NO:381) evidences the presence of the following: a signal peptide from about amino acid 1 to about amino acid 27 and potential N-glycosylation sites from about amino acid 315 to about amino acid 318 and from about amino acid 324 to about amino acid 327. Clone DNA61755-1554 has been deposited with ATCC on August 11, 1998 and is assigned ATCC deposit no. 203112.

- An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence  
15 alignment analysis of the full-length sequence shown in Figure 276 (SEQ ID NO:381), evidenced significant homology between the PRO1287 amino acid sequence and the following Dayhoff sequences: CET24D1\_1, EZRI\_BOVIN, GGU19889\_1, CC3\_YEAST, S74244, NALS\_MOUSE, MOES\_PIG, S28660, S44860 and YNA4\_CAEEL.

20 EXAMPLE 124: Isolation of cDNA clones Encoding Human PRO1312

DNA55773 was identified in a human fetal kidney cDNA library using a yeast screen that preferentially represents the 5' ends of the primary cDNA clones. Based on the DNA55773 sequence, oligonucleotides were synthesized for use as probes to isolate a clone of the full-length coding sequence for PRO1312.

- The full length DNA61873-1574 clone shown in Figure 277 (SEQ ID NO:386) contained a single open  
25 reading frame with an apparent translational initiation site at nucleotide positions 7-9 and ending at the stop codon found at nucleotide positions 643-645. The predicted polypeptide precursor is 212 amino acids long (Figure 278, SEQ ID NO:387). PRO1312 has a calculated molecular weight of approximately 24,024 daltons and an estimated pI of approximately 6.26. Other features include a signal peptide at about amino acids 1-14; a transmembrane domain at about amino acids 141-160, and potential N-glycosylation sites at about amino acids  
30 76-79 and 93-96.

- An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence  
alignment analysis of the full-length sequence shown in Figure 278 (SEQ ID NO:387), revealed some homology between the PRO1312 amino acid sequence and the following Dayhoff sequences: GCINTALPH\_1, GIBMUC1A\_1, P\_R96298, AF001406\_1, PVU88874\_1, P\_R85151, AF041409\_1, CELC50F2\_7, C45875,  
35 and AB009510\_21.

Clone DNA61873-1574 has been deposited with ATCC and is assigned ATCC deposit no. 203132.

EXAMPLE 125: Isolation of cDNA clones Encoding Human PRO1192

A consensus DNA sequence was assembled relative to other EST sequences using phrap as described in Example 1 above. This consensus sequence is designated herein DNA35924. Based on the DNA35924 consensus sequence, oligonucleotides were synthesized: 1) to identify by PCR a cDNA library that contained the sequence of interest, and 2) for use as probes to isolate a clone of the full-length coding sequence for PRO1192.

PCR primers (forward and reverse) were synthesized:

forward PCR primer: 5'-CCGAGGCCATCTAGAGGCCAGAGC-3' (SEQ ID NO:390)

reverse PCR primer: 5'-ACAGGCAGAGCCAATGGCCAGAGC-3' (SEQ ID NO:391).

Additionally, a synthetic oligonucleotide hybridization probe was constructed from the consensus DNA35924 sequence which had the following nucleotide sequence:

hybridization probe:

5'-GAGAGGACTGCGGGAGTTTGGGACCTTTGTGCAGACGTGCTCATG-3' (SEQ ID NO:392).

In order to screen several libraries for a source of a full-length clone, DNA from the libraries was screened by PCR amplification with the PCR primer pair identified above. A positive library was then used to isolate clones encoding the PRO1192 gene using the probe oligonucleotide and one of the PCR primers. RNA for construction of the cDNA libraries was isolated from human fetal liver and spleen tissue.

DNA sequencing of the clones isolated as described above gave the full-length DNA sequence for PRO1192 designated herein as DNA62814-1521 and shown in Figure 279 (SEQ ID NO:388); and the derived protein sequence for PRO1192 which is shown in Figure 280 (SEQ ID NO:389).

The entire coding sequence of PRO1192 is shown in Figure 279 (SEQ ID NO:388). Clone DNA62814-1521 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 121-123 and an apparent stop codon at nucleotide positions 766-768. The predicted polypeptide precursor is 215 amino acids long. The predicted polypeptide precursor has the following features: a signal peptide at about amino acids 1-21; a transmembrane domain at about amino acids 153-176; potential N-glycosylation sites at about amino acids 39-42 and 118-121; and homology with myelin P0 proteins at about amino acids 27-68 and 99-128 of Figure 280. The full-length PRO1192 protein shown in Figure 280 has an estimated molecular weight of about 24,484 daltons and a pI of about 6.98.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 280 (SEQ ID NO:389), revealed homology between the PRO1192 amino acid sequence and the following Dayhoff sequences: GEN12838, MYPO\_HUMAN, AF049498\_1, GEN14531, P\_W14146, HS46KDA\_1, CINB\_RAT, OX2G\_RAT, D87018\_1, and D86996\_2.

Clone DNA62814-1521 was deposited with the ATCC on August 4, 1998, and is assigned ATCC deposit no. 203093.

EXAMPLE 126: Isolation of cDNA clones Encoding Human PRO1160

A consensus DNA sequence was assembled relative to other EST sequences using phrap as described in Example 1 above. This consensus sequence is herein designated DNA40650. Based on the DNA40650 consensus sequence, oligonucleotides were synthesized: 1) to identify by PCR a cDNA library that contained the sequence of interest, and 2) for use as probes to isolate a clone of the full-length coding sequence for PRO1160.

PCR primers (forward and reverse) were synthesized:

forward PCR primer 5'-GCTCCCTGATCTTCATGTCACCACC-3' (SEQ ID NO:395)

reverse PCR primer 5'-CAGGGACACACTCTACCATTCGGGAG-3' (SEQ ID NO:396)

Additionally, a synthetic oligonucleotide hybridization probe was constructed from the consensus DNA40650 sequence which had the following nucleotide sequence

hybridization probe

5'-CCATCTTTCTGGTCTCTGCCCAGAATCCGACAACAGCTGCTC-3' (SEQ ID NO:397)

In order to screen several libraries for a source of a full-length clone, DNA from the libraries was screened by PCR amplification with the PCR primer pair identified above. A positive library was then used to isolate clones encoding the PRO1160 gene using the probe oligonucleotide and one of the PCR primers. RNA for construction of the cDNA libraries was isolated from human breast tissue.

DNA sequencing of the clones isolated as described above gave the full-length DNA sequence for PRO1160 (designated herein as DNA62872-1509 [Figure 281, SEQ ID NO: 393]) and the derived protein sequence for PRO1160.

The entire nucleotide sequence of DNA62872-1509 is shown in Figure 281 (SEQ ID NO:393). Clone DNA62872-1509 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 40-42 and ending at the stop codon at nucleotide positions 310-312 (Figure 281). The predicted polypeptide precursor is 90 amino acids long (Figure 282). The full-length PRO1160 protein shown in Figure 282 has an estimated molecular weight of about 9,039 daltons and a pI of about 4.37. Analysis of the full-length PRO1160 sequence shown in Figure 282 (SEQ ID NO:394) evidences the presence of the following: a signal peptide from about amino acid 1 to about amino acid 19 and a protein kinase C phosphorylation site from about amino acid 68 to about amino acid 70. Clone DNA62872-1509 has been deposited with ATCC on August 4, 1998 and is assigned ATCC deposit no. 203100.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 282 (SEQ ID NO:394), evidenced significant homology between the PRO1160 amino acid sequence and the following Dayhoff sequences: B30305, GEN13490, I53641, S53363, HA34\_BRELC, SP96\_DICDI, S36326, SSU51197\_10, MUC1\_XENLA, TCU32448\_1 and AF000409\_1.

EXAMPLE 127: Isolation of cDNA clones Encoding Human PRO1187

Use of the signal sequence algorithm described in Example 3 above allowed identification of a single EST cluster sequence from the Incyte database. This EST cluster sequence was then compared to a variety of

expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (LIFESEQ®, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altschul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated DNA57726.

In light of an observed sequence homology between the DNA57726 consensus sequence and an EST sequence encompassed within the Incyte EST clone no. 358563, the Incyte EST clone 358563 was purchased and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein. The sequence of this cDNA insert is shown in Figure 283 and is herein designated as DNA62876-1517.

The full length clone shown in Figure 283 contained a single open reading frame with an apparent translational initiation site at nucleotide positions 121-123 and ending at the stop codon found at nucleotide positions 481-483 (Figure 283; SEQ ID NO:398). The predicted polypeptide precursor (Figure 284, SEQ ID NO:399) is 120 amino acids long. The signal peptide is at about amino acids 1-17 of SEQ ID NO:399. PRO1187 has a calculated molecular weight of approximately 12,925 daltons and an estimated pI of approximately 9.46. Clone DNA62876-1517 was deposited with the ATCC on August 4, 1998 and is assigned ATCC deposit no. 203095. It is understood that the deposited clone contains the actual sequence and that the representations herein may have minor sequencing errors.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 284 (SEQ ID NO:399), revealed some sequence identity (and therefore some relation) between the PRO1187 amino acid sequence and the following Dayhoff sequences: MGNENDOBX\_1, CELF41G3\_9, AMPG\_STRLI, HSBBOVHERL\_2, LEEXTEN10\_1, AF029958\_1 and P\_W04957.

#### EXAMPLE 128: Isolation of cDNA clones Encoding Human PRO1185

Use of the signal sequence algorithm described in Example 3 above allowed identification of a single EST cluster sequence from the Incyte database. This EST cluster sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (LIFESEQ®, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altschul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated DNA56426.

In light of an observed sequence homology between the DNA56426 consensus sequence and an EST sequence encompassed within the Incyte EST clone no. 3284411, the Incyte EST clone 3284411 was purchased and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein.

The sequence of this cDNA insert is shown in Figure 285 and is herein designated as DNA62881-1515.

The full length DNA62881-1515 clone shown in Figure 285 contained a single open reading frame with an apparent translational initiation site at nucleotide positions 4-6 and ending at the stop codon found at nucleotide positions 598-600 (Figure 285; SEQ ID NO:400). The predicted polypeptide precursor (Figure 286, SEQ ID NO:401) is 198 amino acids long. The signal peptide is at about amino acids 1-21 of SEQ ID NO:401.

5 PRO1185 has a calculated molecular weight of approximately 22,105 daltons and an estimated pI of approximately 7.73. Clone DNA62881-1515 has been deposited with the ATCC and is assigned ATCC deposit no. 203096.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 286 (SEQ ID NO:401), revealed some sequence identity between the PRO1185 amino acid sequence and the following Dayhoff sequences: TUP1\_YEAST, AF041382\_1, MAOM\_SOLTU, SPPBPHU9\_1, I41024, EPCPLCFAIL\_1, HSPLEC\_1, YKL4\_CAEEL, A44643, TGU65922\_1.

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EXAMPLE 129: Isolation of cDNA clones Encoding Human PRO1345

A consensus DNA sequence was assembled relative to other EST sequences using phrap as described in Example 1 above. This consensus sequence is herein designated DNA47364. Based on the DNA47364 consensus sequence, oligonucleotides were synthesized: 1) to identify by PCR a cDNA library that contained the sequence of interest, and 2) for use as probes to isolate a clone of the full-length coding sequence for PRO1345.

20 PCR primers (forward and reverse) were synthesized:

forward PCR primer 5'-CCTGGTTATCCCCAGGAAGTCCGAC-3' (SEQ ID NO:404)

reverse PCR primer 5'-CTCTTGCTGCTGCGACAGGCCTC-3' (SEQ ID NO:405)

Additionally, a synthetic oligonucleotide hybridization probe was constructed from the consensus DNA47364 sequence which had the following nucleotide sequence

25 hybridization probe

5'-CGCCCTCCAAGACTATGGTAAAAGGAGCCTGCCAGGTGTCAATGAC-3' (SEQ ID NO:406)

In order to screen several libraries for a source of a full-length clone, DNA from the libraries was screened by PCR amplification with the PCR primer pair identified above. A positive library was then used to isolate clones encoding the PRO1345 gene using the probe oligonucleotide and one of the PCR primers. RNA

30 for construction of the cDNA libraries was isolated from human breast carcinoma tissue.

DNA sequencing of the clones isolated as described above gave the full-length DNA sequence for PRO1345 (designated herein as DNA64852-1589 [Figure 287, SEQ ID NO:402]) and the derived protein sequence for PRO1345.

The entire nucleotide sequence of DNA64852-1589 is shown in Figure 287 (SEQ ID NO:402). Clone

35 DNA64852-1589 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 7-9 or 34-36 and ending at the stop codon at nucleotide positions 625-627 (Figure 287). The predicted polypeptide precursor is 206 amino acids long (Figure 288). The full-length PRO1345 protein shown in Figure

288 has an estimated molecular weight of about 23,190 daltons and a pI of about 9.40. Analysis of the full-length PRO1345 sequence shown in Figure 288 (SEQ ID NO:403) evidences the presence of the following: a signal peptide from about amino acid 1 to about amino acid 31 or from about amino acid 10 to about amino acid 31 and a C-type lectin domain signature sequence from about amino acid 176 to about amino acid 190. Clone DNA64852-1589 has been deposited with ATCC on August 18, 1998 and is assigned ATCC deposit no. 203127.

- 5       An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 288 (SEQ ID NO:403), evidenced significant homology between the PRO1345 amino acid sequence and the following Dayhoff sequences: BTU22298\_1, TETN\_CARSP, TETN\_HUMAN, MABA\_RAT, S34198, P\_W13144, MACMBPA\_1, A46274, PSPD\_RAT AND P\_R32188.

10

EXAMPLE 130: Isolation of cDNA clones Encoding Human PRO1245

- Use of the signal sequence algorithm described in Example 3 above allowed identification of a single EST cluster sequence from the Incyte database. This EST cluster sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary
- 15   EST DNA database (LIFESEQ®, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altshul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence
- 20   obtained therefrom is herein designated DNA56019.

In light of an observed sequence homology between the DNA56019 consensus sequence and an EST sequence encompassed within the Incyte EST clone no. 1327836, the Incyte EST clone 1327836 was purchased and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein. The sequence of this cDNA insert is shown in Figure 289 and is herein designated as DNA64884-1527.

- 25       The full length clone shown in Figure 289 contained a single open reading frame with an apparent translational initiation site at nucleotide positions 79-81 and ending at the stop codon found at nucleotide positions 391-393 (Figure 289; SEQ ID NO:407). The predicted polypeptide precursor (Figure 290, SEQ ID NO:408) is 104 amino acids long, with a signal peptide sequence at about amino acid 1 to about amino acid 18. PRO1245 has a calculated molecular weight of approximately 10,100 daltons and an estimated pI of
- 30   approximately 8.76.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 290 (SEQ ID NO:408), revealed some homology between the PRO1245 amino acid sequence and the following Dayhoff sequences: SYA\_THETH, GEN11167, MTV044\_4, AB011151\_1, RLAI2750\_3, SNELIPTRA\_1, S63624, C28391, A37907, and S14064.

- 35       Clone DNA64884-1245 was deposited with the ATCC on August 25, 1998 and is assigned ATCC deposit no. 203155.

**EXAMPLE 131: Isolation of cDNA clones Encoding Human PRO1358**

Use of the signal sequence algorithm described in Example 3 above allowed identification of a single EST cluster sequence from the Incyte database. This EST cluster sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (LIFESEQ®, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altschul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington).

In light of an observed sequence homology between the consensus sequence and an EST sequence encompassed within the Incyte EST clone no. 88718, the Incyte EST clone 88718 was purchased and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein. The sequence of this cDNA insert is shown in Figure 291 and is herein designated as DNA64890-1612.

The full length clone shown in Figure 291 contained a single open reading frame with an apparent translational initiation site at nucleotide positions 86 through 88 and ending at the stop codon found at nucleotide positions 1418 through 1420 (Figure 291; SEQ ID NO:409). The predicted polypeptide precursor (Figure 292, SEQ ID NO:410) is 444 amino acids long. The signal peptide is at about amino acids 1-18 of SEQ ID NO:410. PRO1358 has a calculated molecular weight of approximately 50,719 daltons and an estimated pI of approximately 8.82. Clone DNA64890-1612 was deposited with the ATCC on August 18, 1998 and is assigned ATCC deposit no. 203131.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 292 (SEQ ID NO:410), revealed sequence identity between the PRO1358 amino acid sequence and the following Dayhoff sequences: P\_W07607, AB000545\_1, AB000546\_1, A1AT\_RAT, AB015164\_1, P\_P50021, COTR\_CAVPO, and HAMHPP\_1. The variants claimed in this application exclude these sequences.

**EXAMPLE 132: Isolation of cDNA clones Encoding Human PRO1195**

Use of the signal sequence algorithm described in Example 3 above allowed identification of a single EST cluster sequence from the Incyte database. This EST cluster sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (LIFESEQ®, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altschul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated DNA55716.

In light of an observed sequence homology between the DNA55716 consensus sequence and an EST sequence encompassed within the Incyte EST clone no. 3252980, the Incyte EST clone 3252980 was purchased

and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein. The sequence of this cDNA insert is shown in Figure 293 and is herein designated as DNA65412-1523.

The full length clone shown in Figure 293 contained a single open reading frame with an apparent translational initiation site at nucleotide positions 58-60 and ending at the stop codon found at nucleotide positions 511-513 (Figure 293; SEQ ID NO:411). The predicted polypeptide precursor (Figure 294, SEQ ID NO:412) is 151 amino acids long. The signal sequence is at about amino acids 1-22 of SEQ ID NO:412. PRO1195 has a calculated molecular weight of approximately 17,277 daltons and an estimated pI of approximately 5.33. Clone DNA65412-1523 was deposited with the ATCC on August 4, 1998 and is assigned ATCC deposit no. 203094.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 294 (SEQ ID NO:412), revealed some sequence identity between the PRO1195 amino acid sequence and the following Dayhoff sequences: MMU28486\_1, AF044205\_1, P\_W31186, CELK03C7\_1, F69034, EF1A\_METVA, AF024540\_1, SSU90353\_1, MRSP\_STAAU and P\_R97680.

#### EXAMPLE 133: Isolation of cDNA clones Encoding Human PRO1270

Use of the signal sequence algorithm described in Example 3 above allowed identification of a single EST cluster sequence from the Incyte database. This EST cluster sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (LIFESEQ®, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altschul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated DNA57951.

In light of an observed sequence homology between the DNA57951 consensus sequence and an EST sequence encompassed within the Merck EST clone no. 124878, the Merck EST clone 124878 was purchased and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein. The sequence of this cDNA insert is shown in Figure 295 and is herein designated as DNA66308-1537.

Clone DNA66308-1537 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 103-105 and ending at the stop codon at nucleotide positions 1042-1044 (Figure 295). The predicted polypeptide precursor is 313 amino acids long (Figure 296). The full-length PRO1270 protein shown in Figure 296 has an estimated molecular weight of about 34,978 daltons and a pI of about 5.71. Analysis of the full-length PRO1270 sequence shown in Figure 296 (SEQ ID NO:414) evidences the presence of the following: a signal peptide from about amino acid 1 to about amino acid 16, a potential N-glycosylation site from about amino acid 163 to about amino acid 166 and glycosaminoglycan attachment sites from about amino acid 74 to about amino acid 77 and from about amino acid 289 to about amino acid 292. Clone DNA66308-1537 has been deposited with ATCC on August 25, 1998 and is assigned ATCC deposit no. 203159.



An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 296 (SEQ ID NO:414), evidenced significant homology between the PRO1270 amino acid sequence and the following Dayhoff sequences: XLU86699\_1, S49589, FIBA\_PARPA, FIBB\_HUMAN, P\_R47189, AF004326\_1, DRTENASCN\_1, AF004327\_1, P\_W01411 and FIBG\_BOVIN.

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**EXAMPLE 134: Isolation of cDNA clones Encoding Human PRO1271**

Use of the signal sequence algorithm described in Example 3 above allowed identification of a single EST cluster sequence from the Incyte database. This EST cluster sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (LIFESEQ®, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altschul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated DNA57955.

In light of an observed sequence homology between the DNA57955 consensus sequence and an EST sequence encompassed within the Merck EST clone no. AA625350, the Merck EST clone AA625350 was purchased and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein. The sequence of this cDNA insert is shown in Figure 297 and is herein designated as DNA66309-1538.

Clone DNA66309-1538 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 94-96 and ending at the stop codon at nucleotide positions 718-720 (Figure 297). The predicted polypeptide precursor is 208 amino acids long (Figure 298). The full-length PRO1271 protein shown in Figure 298 has an estimated molecular weight of about 21,531 daltons and a pI of about 8.99. Analysis of the full-length PRO1271 sequence shown in Figure 298 (SEQ ID NO:416) evidences the presence of the following: a signal peptide from about amino acid 1 to about amino acid 31 and a transmembrane domain from about amino acid 166 to about amino acid 187. Clone DNA66309-1538 has been deposited with ATCC on September 15, 1998 and is assigned ATCC deposit no. 203235.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 298 (SEQ ID NO:416), evidenced significant homology between the PRO1271 amino acid sequence and the following Dayhoff sequences: S57180, S63257, AGA1\_YEAST, BPU43599\_1, YS8A\_CAEEL, S67570, LSU54556\_2, S70305, VGLX\_HSVB, and D88733\_1.

**EXAMPLE 135: Isolation of cDNA clones Encoding Human PRO1375**

A Merck/Wash. U. database was searched and a Merck EST was identified. This sequence was then put in a program which aligns it with other sequences from the Swiss-Prot public database, public EST databases (e.g., GenBank, Merck/Wash. U.), and a proprietary EST database (LIFESEQ®, Incyte

Pharmaceuticals, Palo Alto, CA). The search was performed using the computer program BLAST or BLAST2 [Altschul et al., Methods in Enzymology, 266:460-480 (1996)] as a comparison of the extracellular domain (ECD) protein sequences to a 6 frame translation of the EST sequences. Those comparisons resulting in a BLAST score of 70 (or in some cases, 90) or greater that did not encode known proteins were clustered and assembled into consensus DNA sequences with the program "phrap" (Phil Green, University of Washington, Seattle, Washington).

A consensus DNA sequence was assembled relative to other EST sequences using phrap. This consensus sequence is designated herein "DNA67003".

Based on the DNA67003 consensus sequence, the nucleic acid (SEQ ID NO:417) was identified in a human pancreas library. DNA sequencing of the clone gave the full-length DNA sequence for PRO1375 and the derived protein sequence for PRO1375.

The entire coding sequence of PRO1375 is shown in Figure 299 (SEQ ID NO:417). Clone DNA67004-1614 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 104-106 and an apparent stop codon at nucleotide positions 698-700 of SEQ ID NO:417. The predicted polypeptide precursor is 198 amino acids long. The transmembrane domains are at about amino acids 11-28 (type II) and 103-125 of SEQ ID NO:418. Clone DNA67004-1614 has been deposited with ATCC and is assigned ATCC deposit no. 203115. The full-length PRO1375 protein shown in Figure 300 has an estimated molecular weight of about 22,531 daltons and a pI of about 8.47.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 300 (SEQ ID NO:418), revealed sequence identity between the PRO1375 amino acid sequence and the following Dayhoff sequences: AF026198\_5, CELR12C12\_5, S73465, Y011\_MYCPN, S64538\_1, P\_P8150, MUVSHPO10\_1, VSH\_MUMPL and CVU59751\_5.

#### EXAMPLE 136: Isolation of cDNA clones Encoding Human PRO1385

Use of the signal sequence algorithm described in Example 3 above allowed identification of a single EST cluster sequence from the Incyte database. This EST cluster sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (c.g., GenBank) and a proprietary EST DNA database (LIFESEQ®, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altschul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated DNA57952.

In light of an observed sequence homology between the DNA57952 consensus sequence and an EST sequence encompassed within the Incyte EST clone no. 3129630, the Incyte EST clone 3129630 was purchased and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein. The sequence of this cDNA insert is shown in Figure 301 and is herein designated as DNA68869-1610.

Clone DNA68869-1610 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 26-28 and ending at the stop codon at nucleotide positions 410-412 (Figure 301). The predicted polypeptide precursor is 128 amino acids long (Figure 302). The full-length PRO1385 protein shown in Figure 302 has an estimated molecular weight of about 13,663 daltons and a pI of about 10.97. Analysis of the full-length PRO1385 sequence shown in Figure 302 (SEQ ID NO:420) evidences the presence of the following: a signal peptide from about amino acid 1 to about amino acid 28, and glycosylaminoglycan attachment sites from about amino acid 82 to about amino acid 85 and from about amino acid 91 to about amino acid 94. Clone DNA68869-1610 has been deposited with ATCC on August 25, 1998 and is assigned ATCC deposit no. 203164.

- 10 An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 302 (SEQ ID NO:420), evidenced low homology between the PRO1385 amino acid sequence and the following Dayhoff sequences: CELT14A8\_1, LMNACHRA1\_1, HXD9\_HUMAN, CHKCMLF\_1, HS5PP34\_2, DMDRING\_1, A37107\_1, MMLUNGENE\_1, PUM\_DROME and DMU25117\_1.

15 EXAMPLE 137: Isolation of cDNA clones Encoding Human PRO1387

- Use of the signal sequence algorithm described in Example 3 above allowed identification of a single EST cluster sequence from the Incyte database. This EST cluster sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (LIFESEQ®, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altschul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated DNA56259.

- 25 In light of an observed sequence homology between the DNA56259 consensus sequence and an EST sequence encompassed within the Incyte EST clone no. 3507924, the Incyte EST clone 3507924 was purchased and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein. The sequence of this cDNA insert is shown in Figure 303 and is herein designated as DNA68872-1620.

- 30 Clone DNA68872-1620 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 85-87 and ending at the stop codon at nucleotide positions 1267-1269 (Figure 303). The predicted polypeptide precursor is 394 amino acids long (Figure 304). The full-length PRO1387 protein shown in Figure 304 has an estimated molecular weight of about 44,339 daltons and a pI of about 7.10. Analysis of the full-length PRO1387 sequence shown in Figure 304 (SEQ ID NO:422) evidences the presence of the following: a signal peptide from about amino acid 1 to about amino acid 19, a transmembrane domain from about amino acid 275 to about amino acid 296, potential N-glycosylation sites from about amino acid 76 to about amino acid 79, from about amino acid 231 to about amino acid 234, from about amino acid 302 to about amino acid 305, from about amino acid 307 to about amino acid 310 and from about amino acid 376 to about amino acid

379, and amino acid sequence blocks having homology to myelin p0 protein from about amino acid 210 to about amino acid 239 and from about amino acid 92 to about amino acid 121. Clone DNA68872-1620 has been deposited with ATCC on August 25, 1998 and is assigned ATCC deposit no. 203160.

- 5 An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 304 (SEQ ID NO:422), evidenced significant homology between the PRO1387 amino acid sequence and the following Dayhoff sequences: P\_W36955, MYP0\_HETFR, HS46KDA\_1, AF049498\_1, MYOO\_HUMAN, AF030454\_1, A53268, SHPTCRA\_1, P\_W14146 and GEN12838.

EXAMPLE 138: Isolation of cDNA clones Encoding Human PRO1384

- 10 A consensus DNA sequence was assembled relative to other EST sequences using phrap as described in Example 1 above. This consensus sequence is herein designated DNA54192. Based on the DNA54192 sequence, oligonucleotides were synthesized: 1) to identify by PCR a cDNA library that contained the sequence of interest, and 2) for use as probes to isolate a clone of the full-length coding sequence for PRO1384.

PCR primers (forward and reverse) were synthesized:

- 15 forward PCR primer 5'-TGCAGCCCCTGTGACACAACTGG-3' (SEQ ID NO:425)  
reverse PCR primer 5'-CTGAGATAACCGAGCCATCCTCCAC-3' (SEQ ID NO:426)

Additionally, a synthetic oligonucleotide hybridization probe was constructed from the DNA54192 sequence which had the following nucleotide sequence:

hybridization probe

- 20 5'-GGAGATAGCTGCTATGGGTTCTTCAGGCACAACCTTAACATGGGAAG-3' (SEQ ID NO:427)

In order to screen several libraries for a source of a full-length clone, DNA from the libraries was screened by PCR amplification with the PCR primer pair identified above. A positive library was then used to isolate clones encoding the PRO1384 gene using the probe oligonucleotide and one of the PCR primers. RNA for construction of the cDNA libraries was isolated from human fetal liver.

- 25 DNA sequencing of the clones isolated as described above gave the full-length DNA sequence for PRO1384 (designated herein as DNA71159-1617 [Figure 305, SEQ ID NO:423]; and the derived protein sequence for PRO1384.

- The entire coding sequence of PRO1384 is shown in Figure 305 (SEQ ID NO:423). Clone DNA71159-1617 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 182-184 and an apparent stop codon at nucleotide positions 869-871. The predicted polypeptide precursor is 229 amino acids long. The full-length PRO1384 protein shown in Figure 306 has an estimated molecular weight of about 26,650 daltons and a pI of about 8.76. Additional features include a type II transmembrane domain at about amino acids 32-57, and potential N-glycosylation sites at about amino acids 68-71, 120-123, and 134-137.

- 35 An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 306 (SEQ ID NO:424), revealed homology between the PRO1384 amino acid sequence and the following Dayhoff sequences: AF054819\_1, HSAJ1687\_1, AF009511\_1, AB010710\_1, GEN13595, HSAJ673\_1, GEN13961, AB005900\_1, LECH\_CHICK, AF021349\_1,

and NK13\_RAT.

Clone DNA71159-1617 has been deposited with ATCC and is assigned ATCC deposit no. 203135.

EXAMPLE 139: Use of PRO as a hybridization probe

5 The following method describes use of a nucleotide sequence encoding PRO as a hybridization probe. DNA comprising the coding sequence of full-length or mature PRO as disclosed herein is employed as a probe to screen for homologous DNAs (such as those encoding naturally-occurring variants of PRO) in human tissue cDNA libraries or human tissue genomic libraries.

10 Hybridization and washing of filters containing either library DNAs is performed under the following high stringency conditions. Hybridization of radiolabeled PRO-derived probe to the filters is performed in a solution of 50% formamide, 5x SSC, 0.1% SDS, 0.1% sodium pyrophosphate, 50 mM sodium phosphate, pH 6.8, 2x Denhardt's solution, and 10% dextran sulfate at 42°C for 20 hours. Washing of the filters is performed in an aqueous solution of 0.1x SSC and 0.1% SDS at 42°C.

15 DNAs having a desired sequence identity with the DNA encoding full-length native sequence PRO can then be identified using standard techniques known in the art.

EXAMPLE 140: Expression of PRO in *E. coli*

This example illustrates preparation of an unglycosylated form of PRO by recombinant expression in *E. coli*.

20 The DNA sequence encoding PRO is initially amplified using selected PCR primers. The primers should contain restriction enzyme sites which correspond to the restriction enzyme sites on the selected expression vector. A variety of expression vectors may be employed. An example of a suitable vector is pBR322 (derived from *E. coli*; see Bolivar et al., Gene, 2:95 (1977)) which contains genes for ampicillin and tetracycline resistance. The vector is digested with restriction enzyme and dephosphorylated. The PCR amplified sequences are then ligated into the vector. The vector will preferably include sequences which encode  
25 for an antibiotic resistance gene, a trp promoter, a polyhis leader (including the first six STII codons, polyhis sequence, and enterokinase cleavage site), the PRO coding region, lambda transcriptional terminator, and an argU gene.

30 The ligation mixture is then used to transform a selected *E. coli* strain using the methods described in Sambrook et al., supra. Transformants are identified by their ability to grow on LB plates and antibiotic resistant colonies are then selected. Plasmid DNA can be isolated and confirmed by restriction analysis and DNA sequencing.

Selected clones can be grown overnight in liquid culture medium such as LB broth supplemented with antibiotics. The overnight culture may subsequently be used to inoculate a larger scale culture. The cells are then grown to a desired optical density, during which the expression promoter is turned on.

35 After culturing the cells for several more hours, the cells can be harvested by centrifugation. The cell pellet obtained by the centrifugation can be solubilized using various agents known in the art, and the solubilized PRO protein can then be purified using a metal chelating column under conditions that allow tight binding of the

protein.

PRO may be expressed in *E. coli* in a poly-His tagged form, using the following procedure. The DNA encoding PRO is initially amplified using selected PCR primers. The primers will contain restriction enzyme sites which correspond to the restriction enzyme sites on the selected expression vector, and other useful sequences providing for efficient and reliable translation initiation, rapid purification on a metal chelation column, and proteolytic removal with enterokinase. The PCR-amplified, poly-His tagged sequences are then ligated into an expression vector, which is used to transform an *E. coli* host based on strain 52 (W3110 fuhA(tonA) lon galE rpoHts(htpRts) clpP(lacIq). Transformants are first grown in LB containing 50 mg/ml carbenicillin at 30°C with shaking until an O.D.600 of 3-5 is reached. Cultures are then diluted 50-100 fold into CRAP media (prepared by mixing 3.57 g (NH<sub>4</sub>)<sub>2</sub>SO<sub>4</sub>, 0.71 g sodium citrate•2H<sub>2</sub>O, 1.07 g KCl, 5.36 g Difco yeast extract, 5.36 g Sheffield hycase SF in 500 mL water, as well as 110 mM MPOS, pH 7.3, 0.55% (w/v) glucose and 7 mM MgSO<sub>4</sub>) and grown for approximately 20-30 hours at 30°C with shaking. Samples are removed to verify expression by SDS-PAGE analysis, and the bulk culture is centrifuged to pellet the cells. Cell pellets are frozen until purification and refolding.

*E. coli* paste from 0.5 to 1 L fermentations (6-10 g pellets) is resuspended in 10 volumes (w/v) in 7 M guanidine, 20 mM Tris, pH 8 buffer. Solid sodium sulfite and sodium tetrathionate is added to make final concentrations of 0.1M and 0.02 M, respectively, and the solution is stirred overnight at 4°C. This step results in a denatured protein with all cysteine residues blocked by sulfitolization. The solution is centrifuged at 40,000 rpm in a Beckman Ultracentrifuge for 30 min. The supernatant is diluted with 3-5 volumes of metal chelate column buffer (6 M guanidine, 20 mM Tris, pH 7.4) and filtered through 0.22 micron filters to clarify. The clarified extract is loaded onto a 5 ml Qiagen Ni-NTA metal chelate column equilibrated in the metal chelate column buffer. The column is washed with additional buffer containing 50 mM imidazole (Calbiochem, Utrol grade), pH 7.4. The protein is eluted with buffer containing 250 mM imidazole. Fractions containing the desired protein are pooled and stored at 4°C. Protein concentration is estimated by its absorbance at 280 nm using the calculated extinction coefficient based on its amino acid sequence.

The proteins are refolded by diluting the sample slowly into freshly prepared refolding buffer consisting of: 20 mM Tris, pH 8.6, 0.3 M NaCl, 2.5 M urea, 5 mM cysteine, 20 mM glycine and 1 mM EDTA. Refolding volumes are chosen so that the final protein concentration is between 50 to 100 micrograms/ml. The refolding solution is stirred gently at 4°C for 12-36 hours. The refolding reaction is quenched by the addition of TFA to a final concentration of 0.4% (pH of approximately 3). Before further purification of the protein, the solution is filtered through a 0.22 micron filter and acetonitrile is added to 2-10% final concentration. The refolded protein is chromatographed on a Poros R1/H reversed phase column using a mobile buffer of 0.1% TFA with elution with a gradient of acetonitrile from 10 to 80%. Aliquots of fractions with A280 absorbance are analyzed on SDS polyacrylamide gels and fractions containing homogeneous refolded protein are pooled. Generally, the properly refolded species of most proteins are eluted at the lowest concentrations of acetonitrile since those species are the most compact with their hydrophobic interiors shielded from interaction with the reversed phase resin. Aggregated species are usually eluted at higher acetonitrile concentrations. In addition to resolving misfolded forms of proteins from the desired form, the reversed phase step also removes endotoxin

from the samples.

Fractions containing the desired folded PRO polypeptide are pooled and the acetonitrile removed using a gentle stream of nitrogen directed at the solution. Proteins are formulated into 20 mM Hepes, pH 6.8 with 0.14 M sodium chloride and 4% mannitol by dialysis or by gel filtration using G25 Superfine (Pharmacia) resins equilibrated in the formulation buffer and sterile filtered.

- 5 Many of the PRO polypeptides disclosed herein were successfully expressed as described above.

#### EXAMPLE 141: Expression of PRO in mammalian cells

This example illustrates preparation of a potentially glycosylated form of PRO by recombinant expression in mammalian cells.

- 10 The vector, pRK5 (see EP 307,247, published March 15, 1989), is employed as the expression vector. Optionally, the PRO DNA is ligated into pRK5 with selected restriction enzymes to allow insertion of the PRO DNA using ligation methods such as described in Sambrook et al., *supra*. The resulting vector is called pRK5-PRO.

- 15 In one embodiment, the selected host cells may be 293 cells. Human 293 cells (ATCC CCL 1573) are grown to confluence in tissue culture plates in medium such as DMEM supplemented with fetal calf serum and optionally, nutrient components and/or antibiotics. About 10  $\mu$ g pRK5-PRO DNA is mixed with about 1  $\mu$ g DNA encoding the VA RNA gene [Thimmappaya et al., *Cell*, 31:543 (1982)] and dissolved in 500  $\mu$ l of 1 mM Tris-HCl, 0.1 mM EDTA, 0.227 M  $\text{CaCl}_2$ . To this mixture is added, dropwise, 500  $\mu$ l of 50 mM HEPES (pH 7.35), 280 mM NaCl, 1.5 mM  $\text{NaPO}_4$ , and a precipitate is allowed to form for 10 minutes at 25°C. The precipitate is suspended and added to the 293 cells and allowed to settle for about four hours at 37°C. The culture medium is aspirated off and 2 ml of 20% glycerol in PBS is added for 30 seconds. The 293 cells are then washed with serum free medium, fresh medium is added and the cells are incubated for about 5 days.

- 25 Approximately 24 hours after the transfections, the culture medium is removed and replaced with culture medium (alone) or culture medium containing 200  $\mu\text{Ci/ml}$   $^{35}\text{S}$ -cysteine and 200  $\mu\text{Ci/ml}$   $^{35}\text{S}$ -methionine. After a 12 hour incubation, the conditioned medium is collected, concentrated on a spin filter, and loaded onto a 15% SDS gel. The processed gel may be dried and exposed to film for a selected period of time to reveal the presence of PRO polypeptide. The cultures containing transfected cells may undergo further incubation (in serum free medium) and the medium is tested in selected bioassays.

- 30 In an alternative technique, PRO may be introduced into 293 cells transiently using the dextran sulfate method described by Sompayrac et al., *Proc. Natl. Acad. Sci.*, 12:7575 (1981). 293 cells are grown to maximal density in a spinner flask and 700  $\mu$ g pRK5-PRO DNA is added. The cells are first concentrated from the spinner flask by centrifugation and washed with PBS. The DNA-dextran precipitate is incubated on the cell pellet for four hours. The cells are treated with 20% glycerol for 90 seconds, washed with tissue culture medium, and re-introduced into the spinner flask containing tissue culture medium, 5  $\mu\text{g/ml}$  bovine insulin and 35 0.1  $\mu\text{g/ml}$  bovine transferrin. After about four days, the conditioned media is centrifuged and filtered to remove cells and debris. The sample containing expressed PRO can then be concentrated and purified by any selected method, such as dialysis and/or column chromatography.

In another embodiment, PRO can be expressed in CHO cells. The pRK5-PRO can be transfected into CHO cells using known reagents such as  $\text{CaPO}_4$  or DEAE-dextran. As described above, the cell cultures can be incubated, and the medium replaced with culture medium (alone) or medium containing a radiolabel such as  $^{35}\text{S}$ -methionine. After determining the presence of PRO polypeptide, the culture medium may be replaced with serum free medium. Preferably, the cultures are incubated for about 6 days, and then the conditioned medium is harvested. The medium containing the expressed PRO can then be concentrated and purified by any selected method.

Epitope-tagged PRO may also be expressed in host CHO cells. The PRO may be subcloned out of the pRK5 vector. The subclone insert can undergo PCR to fuse in frame with a selected epitope tag such as a poly-his tag into a Baculovirus expression vector. The poly-his tagged PRO insert can then be subcloned into a SV40 driven vector containing a selection marker such as DHFR for selection of stable clones. Finally, the CHO cells can be transfected (as described above) with the SV40 driven vector. Labeling may be performed, as described above, to verify expression. The culture medium containing the expressed poly-His tagged PRO can then be concentrated and purified by any selected method, such as by  $\text{Ni}^{2+}$ -chelate affinity chromatography.

PRO may also be expressed in CHO and/or COS cells by a transient expression procedure or in CHO cells by another stable expression procedure.

Stable expression in CHO cells is performed using the following procedure. The proteins are expressed as an IgG construct (immunoadhesin), in which the coding sequences for the soluble forms (e.g. extracellular domains) of the respective proteins are fused to an IgG1 constant region sequence containing the hinge, CH2 and CH2 domains and/or is a poly-His tagged form.

Following PCR amplification, the respective DNAs are subcloned in a CHO expression vector using standard techniques as described in Ausubel et al., Current Protocols of Molecular Biology, Unit 3.16, John Wiley and Sons (1997). CHO expression vectors are constructed to have compatible restriction sites 5' and 3' of the DNA of interest to allow the convenient shuttling of cDNA's. The vector used expression in CHO cells is as described in Lucas et al., Nucl. Acids Res. 24:9 (1774-1779 (1996), and uses the SV40 early promoter/enhancer to drive expression of the cDNA of interest and dihydrofolate reductase (DHFR). DHFR expression permits selection for stable maintenance of the plasmid following transfection.

Twelve micrograms of the desired plasmid DNA is introduced into approximately 10 million CHO cells using commercially available transfection reagents Superfect<sup>®</sup> (Quiagen), Dosper<sup>®</sup> or Fugene<sup>®</sup> (Boehringer Mannheim). The cells are grown as described in Lucas et al., supra. Approximately  $3 \times 10^7$  cells are frozen in an ampule for further growth and production as described below.

The ampules containing the plasmid DNA are thawed by placement into water bath and mixed by vortexing. The contents are pipetted into a centrifuge tube containing 10 mLs of media and centrifuged at 1000 rpm for 5 minutes. The supernatant is aspirated and the cells are resuspended in 10 mL of selective media (0.2  $\mu\text{m}$  filtered PS20 with 5% 0.2  $\mu\text{m}$  diafiltered fetal bovine serum). The cells are then aliquoted into a 100 mL spinner containing 90 mL of selective media. After 1-2 days, the cells are transferred into a 250 mL spinner filled with 150 mL selective growth medium and incubated at 37°C. After another 2-3 days, 250 mL, 500 mL and 2000 mL spinners are seeded with  $3 \times 10^5$  cells/mL. The cell media is exchanged with fresh media by



centrifugation and resuspension in production medium. Although any suitable CHO media may be employed, a production medium described in U.S. Patent No. 5,122,469, issued June 16, 1992 may actually be used. A 3L production spinner is seeded at  $1.2 \times 10^6$  cells/mL. On day 0, the cell number pH is determined. On day 1, the spinner is sampled and sparging with filtered air is commenced. On day 2, the spinner is sampled, the temperature shifted to 33°C, and 30 mL of 500 g/L glucose and 0.6 mL of 10% antifoam (e.g., 35% polydimethylsiloxane emulsion, Dow Corning 365 Medical Grade Emulsion) taken. Throughout the production, the pH is adjusted as necessary to keep it at around 7.2. After 10 days, or until the viability dropped below 70%, the cell culture is harvested by centrifugation and filtering through a 0.22  $\mu$ m filter. The filtrate was either stored at 4°C or immediately loaded onto columns for purification.

For the poly-His tagged constructs, the proteins are purified using a Ni-NTA column (Qiagen). Before purification, imidazole is added to the conditioned media to a concentration of 5 mM. The conditioned media is pumped onto a 6 ml Ni-NTA column equilibrated in 20 mM Hepes, pH 7.4, buffer containing 0.3 M NaCl and 5 mM imidazole at a flow rate of 4-5 ml/min. at 4°C. After loading, the column is washed with additional equilibration buffer and the protein eluted with equilibration buffer containing 0.25 M imidazole. The highly purified protein is subsequently desalted into a storage buffer containing 10 mM Hepes, 0.14 M NaCl and 4% mannitol, pH 6.8, with a 25 ml G25 Superfine (Pharmacia) column and stored at -80°C.

Immunoadhesin (Fc-containing) constructs are purified from the conditioned media as follows. The conditioned medium is pumped onto a 5 ml Protein A column (Pharmacia) which had been equilibrated in 20 mM Na phosphate buffer, pH 6.8. After loading, the column is washed extensively with equilibration buffer before elution with 100 mM citric acid, pH 3.5. The eluted protein is immediately neutralized by collecting 1 ml fractions into tubes containing 275  $\mu$ L of 1 M Tris buffer, pH 9. The highly purified protein is subsequently desalted into storage buffer as described above for the poly-His tagged proteins. The homogeneity is assessed by SDS polyacrylamide gels and by N-terminal amino acid sequencing by Edman degradation.

Many of the PRO polypeptides disclosed herein were successfully expressed as described above.

#### 25 EXAMPLE 142: Expression of PRO in Yeast

The following method describes recombinant expression of PRO in yeast.

First, yeast expression vectors are constructed for intracellular production or secretion of PRO from the ADH2/GAPDH promoter. DNA encoding PRO and the promoter is inserted into suitable restriction enzyme sites in the selected plasmid to direct intracellular expression of PRO. For secretion, DNA encoding PRO can be cloned into the selected plasmid, together with DNA encoding the ADH2/GAPDH promoter, a native PRO signal peptide or other mammalian signal peptide, or, for example, a yeast alpha-factor or invertase secretory signal/leader sequence, and linker sequences (if needed) for expression of PRO.

Yeast cells, such as yeast strain AB110, can then be transformed with the expression plasmids described above and cultured in selected fermentation media. The transformed yeast supernatants can be analyzed by precipitation with 10% trichloroacetic acid and separation by SDS-PAGE, followed by staining of the gels with Coomassie Blue stain.

Recombinant PRO can subsequently be isolated and purified by removing the yeast cells from the fermentation medium by centrifugation and then concentrating the medium using selected cartridge filters. The concentrate containing PRO may further be purified using selected column chromatography resins.

Many of the PRO polypeptides disclosed herein were successfully expressed as described above.

#### 5 EXAMPLE 143: Expression of PRO in Baculovirus-Infected Insect Cells

The following method describes recombinant expression of PRO in Baculovirus-infected insect cells.

The sequence coding for PRO is fused upstream of an epitope tag contained within a baculovirus expression vector. Such epitope tags include poly-his tags and immunoglobulin tags (like Fc regions of IgG). A variety of plasmids may be employed, including plasmids derived from commercially available plasmids such as pVL1393 (Novagen). Briefly, the sequence encoding PRO or the desired portion of the coding sequence of PRO such as the sequence encoding the extracellular domain of a transmembrane protein or the sequence encoding the mature protein if the protein is extracellular is amplified by PCR with primers complementary to the 5' and 3' regions. The 5' primer may incorporate flanking (selected) restriction enzyme sites. The product is then digested with those selected restriction enzymes and subcloned into the expression vector.

15 Recombinant baculovirus is generated by co-transfecting the above plasmid and BaculoGold™ virus DNA (Pharmingen) into *Spodoptera frugiperda* ("Sf9") cells (ATCC CRL 1711) using lipofectin (commercially available from GIBCO-BRL). After 4 - 5 days of incubation at 28°C, the released viruses are harvested and used for further amplifications. Viral infection and protein expression are performed as described by O'Reilley et al., Baculovirus expression vectors: A Laboratory Manual, Oxford: Oxford University Press (1994).

20 Expressed poly-his tagged PRO can then be purified, for example, by Ni<sup>2+</sup>-chelate affinity chromatography as follows. Extracts are prepared from recombinant virus-infected Sf9 cells as described by Rupert et al., Nature, 362:175-179 (1993). Briefly, Sf9 cells are washed, resuspended in sonication buffer (25 mL Hepes, pH 7.9; 12.5 mM MgCl<sub>2</sub>; 0.1 mM EDTA; 10% glycerol; 0.1% NP-40; 0.4 M KCl), and sonicated twice for 20 seconds on ice. The sonicates are cleared by centrifugation, and the supernatant is diluted 50-fold in loading buffer (50 mM phosphate, 300 mM NaCl, 10% glycerol, pH 7.8) and filtered through a 0.45 μm filter. A Ni<sup>2+</sup>-NTA agarose column (commercially available from Qiagen) is prepared with a bed volume of 5 mL, washed with 25 mL of water and equilibrated with 25 mL of loading buffer. The filtered cell extract is loaded onto the column at 0.5 mL per minute. The column is washed to baseline A<sub>280</sub> with loading buffer, at which point fraction collection is started. Next, the column is washed with a secondary wash buffer (50 mM phosphate; 300 mM NaCl, 10% glycerol, pH 6.0), which elutes nonspecifically bound protein. After reaching A<sub>280</sub> baseline again, the column is developed with a 0 to 500 mM Imidazole gradient in the secondary wash buffer. One mL fractions are collected and analyzed by SDS-PAGE and silver staining or Western blot with Ni<sup>2+</sup>-NTA-conjugated to alkaline phosphatase (Qiagen). Fractions containing the eluted His<sub>10</sub>-tagged PRO are pooled and dialyzed against loading buffer.

35 Alternatively, purification of the IgG tagged (or Fc tagged) PRO can be performed using known chromatography techniques, including for instance, Protein A or protein G column chromatography.

Many of the PRO polypeptides disclosed herein were successfully expressed as described above.

EXAMPLE 144: Preparation of Antibodies that Bind PRO

This example illustrates preparation of monoclonal antibodies which can specifically bind PRO.

Techniques for producing the monoclonal antibodies are known in the art and are described, for instance, in Goding, *supra*. Immunogens that may be employed include purified PRO, fusion proteins containing PRO, and cells expressing recombinant PRO on the cell surface. Selection of the immunogen can be made by the skilled artisan without undue experimentation.

Mice, such as Balb/c, are immunized with the PRO immunogen emulsified in complete Freund's adjuvant and injected subcutaneously or intraperitoneally in an amount from 1-100 micrograms. Alternatively, the immunogen is emulsified in MPL-TDM adjuvant (Ribi Immunochemical Research, Hamilton, MT) and injected into the animal's hind foot pads. The immunized mice are then boosted 10 to 12 days later with additional immunogen emulsified in the selected adjuvant. Thereafter, for several weeks, the mice may also be boosted with additional immunization injections. Serum samples may be periodically obtained from the mice by retro-orbital bleeding for testing in ELISA assays to detect anti-PRO antibodies.

After a suitable antibody titer has been detected, the animals "positive" for antibodies can be injected with a final intravenous injection of PRO. Three to four days later, the mice are sacrificed and the spleen cells are harvested. The spleen cells are then fused (using 35% polyethylene glycol) to a selected murine myeloma cell line such as P3X63AgU.1, available from ATCC, No. CRL 1597. The fusions generate hybridoma cells which can then be plated in 96 well tissue culture plates containing HAT (hypoxanthine, aminopterin, and thymidine) medium to inhibit proliferation of non-fused cells, myeloma hybrids, and spleen cell hybrids.

The hybridoma cells will be screened in an ELISA for reactivity against PRO. Determination of "positive" hybridoma cells secreting the desired monoclonal antibodies against PRO is within the skill in the art.

The positive hybridoma cells can be injected intraperitoneally into syngeneic Balb/c mice to produce ascites containing the anti-PRO monoclonal antibodies. Alternatively, the hybridoma cells can be grown in tissue culture flasks or roller bottles. Purification of the monoclonal antibodies produced in the ascites can be accomplished using ammonium sulfate precipitation, followed by gel exclusion chromatography. Alternatively, affinity chromatography based upon binding of antibody to protein A or protein G can be employed.

EXAMPLE 145: Purification of PRO Polypeptides Using Specific Antibodies

Native or recombinant PRO polypeptides may be purified by a variety of standard techniques in the art of protein purification. For example, pro-PRO polypeptide, mature PRO polypeptide, or pre-PRO polypeptide is purified by immunoaffinity chromatography using antibodies specific for the PRO polypeptide of interest. In general, an immunoaffinity column is constructed by covalently coupling the anti-PRO polypeptide antibody to an activated chromatographic resin.

Polyclonal immunoglobulins are prepared from immune sera either by precipitation with ammonium sulfate or by purification on immobilized Protein A (Pharmacia LKB Biotechnology, Piscataway, N.J.). Likewise, monoclonal antibodies are prepared from mouse ascites fluid by ammonium sulfate precipitation or chromatography on immobilized Protein A. Partially purified immunoglobulin is covalently attached to a chromatographic resin such as CnBr-activated SEPHAROSE™ (Pharmacia LKB Biotechnology). The antibody

is coupled to the resin, the resin is blocked, and the derivative resin is washed according to the manufacturer's instructions.

Such an immunoaffinity column is utilized in the purification of PRO polypeptide by preparing a fraction from cells containing PRO polypeptide in a soluble form. This preparation is derived by solubilization of the whole cell or of a subcellular fraction obtained via differential centrifugation by the addition of detergent or by other methods well known in the art. Alternatively, soluble PRO polypeptide containing a signal sequence may be secreted in useful quantity into the medium in which the cells are grown.

A soluble PRO polypeptide-containing preparation is passed over the immunoaffinity column, and the column is washed under conditions that allow the preferential absorbance of PRO polypeptide (*e.g.*, high ionic strength buffers in the presence of detergent). Then, the column is eluted under conditions that disrupt antibody/PRO polypeptide binding (*e.g.*, a low pH buffer such as approximately pH 2-3, or a high concentration of a chaotrope such as urea or thiocyanate ion), and PRO polypeptide is collected.

#### EXAMPLE 146: Drug Screening

This invention is particularly useful for screening compounds by using PRO polypeptides or binding fragment thereof in any of a variety of drug screening techniques. The PRO polypeptide or fragment employed in such a test may either be free in solution, affixed to a solid support, borne on a cell surface, or located intracellularly. One method of drug screening utilizes eukaryotic or prokaryotic host cells which are stably transformed with recombinant nucleic acids expressing the PRO polypeptide or fragment. Drugs are screened against such transformed cells in competitive binding assays. Such cells, either in viable or fixed form, can be used for standard binding assays. One may measure, for example, the formation of complexes between PRO polypeptide or a fragment and the agent being tested. Alternatively, one can examine the diminution in complex formation between the PRO polypeptide and its target cell or target receptors caused by the agent being tested.

Thus, the present invention provides methods of screening for drugs or any other agents which can affect a PRO polypeptide-associated disease or disorder. These methods comprise contacting such an agent with an PRO polypeptide or fragment thereof and assaying (i) for the presence of a complex between the agent and the PRO polypeptide or fragment, or (ii) for the presence of a complex between the PRO polypeptide or fragment and the cell, by methods well known in the art. In such competitive binding assays, the PRO polypeptide or fragment is typically labeled. After suitable incubation, free PRO polypeptide or fragment is separated from that present in bound form, and the amount of free or uncomplexed label is a measure of the ability of the particular agent to bind to PRO polypeptide or to interfere with the PRO polypeptide/cell complex.

Another technique for drug screening provides high throughput screening for compounds having suitable binding affinity to a polypeptide and is described in detail in WO 84/03564, published on September 13, 1984. Briefly stated, large numbers of different small peptide test compounds are synthesized on a solid substrate, such as plastic pins or some other surface. As applied to a PRO polypeptide, the peptide test compounds are reacted with PRO polypeptide and washed. Bound PRO polypeptide is detected by methods well known in the art. Purified PRO polypeptide can also be coated directly onto plates for use in the aforementioned drug screening techniques. In addition, non-neutralizing antibodies can be used to capture the peptide and immobilize it on the

solid support.

This invention also contemplates the use of competitive drug screening assays in which neutralizing antibodies capable of binding PRO polypeptide specifically compete with a test compound for binding to PRO polypeptide or fragments thereof. In this manner, the antibodies can be used to detect the presence of any peptide which shares one or more antigenic determinants with PRO polypeptide.

5

EXAMPLE 147: Rational Drug Design

The goal of rational drug design is to produce structural analogs of biologically active polypeptide of interest (*i.e.*, a PRO polypeptide) or of small molecules with which they interact, *e.g.*, agonists, antagonists, or inhibitors. Any of these examples can be used to fashion drugs which are more active or stable forms of the PRO polypeptide or which enhance or interfere with the function of the PRO polypeptide *in vivo* (*c.f.*, Hodgson, Bio/Technology, 9: 19-21 (1991)).

In one approach, the three-dimensional structure of the PRO polypeptide, or of an PRO polypeptide-inhibitor complex, is determined by x-ray crystallography, by computer modeling or, most typically, by a combination of the two approaches. Both the shape and charges of the PRO polypeptide must be ascertained to elucidate the structure and to determine active site(s) of the molecule. Less often, useful information regarding the structure of the PRO polypeptide may be gained by modeling based on the structure of homologous proteins. In both cases, relevant structural information is used to design analogous PRO polypeptide-like molecules or to identify efficient inhibitors. Useful examples of rational drug design may include molecules which have improved activity or stability as shown by Braxton and Wells, Biochemistry, 31:7796-7801 (1992) or which act as inhibitors, agonists, or antagonists of native peptides as shown by Athauda *et al.*, J. Biochem., 113:742-746 (1993).

It is also possible to isolate a target-specific antibody, selected by functional assay, as described above, and then to solve its crystal structure. This approach, in principle, yields a pharmacore upon which subsequent drug design can be based. It is possible to bypass protein crystallography altogether by generating anti-idiotypic antibodies (anti-ids) to a functional, pharmacologically active antibody. As a mirror image of a mirror image, the binding site of the anti-ids would be expected to be an analog of the original receptor. The anti-id could then be used to identify and isolate peptides from banks of chemically or biologically produced peptides. The isolated peptides would then act as the pharmacore.

By virtue of the present invention, sufficient amounts of the PRO polypeptide may be made available to perform such analytical studies as X-ray crystallography. In addition, knowledge of the PRO polypeptide amino acid sequence provided herein will provide guidance to those employing computer modeling techniques in place of or in addition to x-ray crystallography.

35

Deposit of Material

The following materials have been deposited with the American Type Culture Collection, 10801 University Blvd., Manassas, VA 20110-2209, USA (ATCC):

Table 2

<u>5</u>	<u>Material</u>	<u>ATCC Dep. No.</u>	<u>Deposit Date</u>
	DNA16422-1209	209929	June 2, 1998
	DNA16435-1208	209930	June 2, 1998
	DNA21624-1391	209917	June 2, 1998
	DNA23334-1392	209918	June 2, 1998
10	DNA26288-1239	209792	April 21, 1998
	DNA26843-1389	203099	August 4, 1998
	DNA26844-1394	209926	June 2, 1998
	DNA30862-1396	209920	June 2, 1998
	DNA35680-1212	209790	April 21, 1998
15	DNA40621-1440	209922	June 2, 1998
	DNA44161-1434	209907	May 27, 1998
	DNA44694-1500	203114	August 11, 1998
	DNA45495-1550	203156	August 25, 1998
	DNA47361-1154	209431	November 7, 1997
20	DNA47394-1572	203109	August 11, 1998
	DNA48320-1433	209904	May 27, 1998
	DNA48334-1435	209924	June 2, 1998
	DNA48606-1479	203040	July 1, 1998
	DNA49141-1431	203003	June 23, 1998
25	DNA49142-1430	203002	June 23, 1998
	DNA49143-1429	203013	June 23, 1998
	DNA49647-1398	209919	June 2, 1998
	DNA49819-1439	209931	June 2, 1998
	DNA49820-1427	209932	June 2, 1998
30	DNA49821-1562	209981	June 16, 1998
	DNA52192-1369	203042	July 1, 1998
	DNA52598-1518	203107	August 11, 1998
	DNA53913-1490	203162	August 25, 1998
	DNA53978-1443	209983	June 16, 1998
35	DNA53996-1442	209921	June 2, 1998
	DNA56041-1416	203012	June 23, 1998
	DNA56047-1456	209948	June 9, 1998
	DNA56050-1455	203011	June 23, 1998
	DNA56110-1437	203113	August 11, 1998
40	DNA56113-1378	203049	July 1, 1998
	DNA56410-1414	209923	June 2, 1998
	DNA56436-1448	209902	May 27, 1998
	DNA56855-1447	203004	June 23, 1998
	DNA56859-1445	203019	June 23, 1998
45	DNA56860-1510	209952	June 9, 1998
	DNA56865-1491	203022	June 23, 1998
	DNA56866-1342	203023	June 23, 1998
	DNA56868-1209	203024	June 23, 1998
	DNA56869-1545	203161	August 25, 1998
50	DNA56870-1492	209925	June 2, 1998
	DNA57033-1403	209905	May 27, 1998
	DNA57037-1444	209903	May 27, 1998
	DNA57129-1413	209977	June 16, 1998

	DNA57690-1374	209950	June 9, 1998
	DNA57693-1424	203008	June 23, 1998
	DNA57694-1341	203017	June 23, 1998
	DNA57695-1340	203006	June 23, 1998
	DNA57699-1412	203020	June 23, 1998
5	DNA57702-1476	209951	June 9, 1998
	DNA57704-1452	209953	June 9, 1998
	DNA57708-1411	203021	June 23, 1998
	DNA57710-1451	203048	July 1, 1998
	DNA57711-1501	203047	July 1, 1998
10	DNA57827-1493	203045	July 1, 1998
	DNA57834-1339	209954	June 9, 1998
	DNA57836-1338	203025	June 23, 1998
	DNA57838-1337	203014	June 23, 1998
	DNA57844-1410	203010	June 23, 1998
15	DNA58721-1475	203110	August 11, 1998
	DNA58723-1588	203133	August 18, 1998
	DNA58737-1473	203136	August 18, 1998
	DNA58743-1609	203154	August 25, 1998
	DNA58846-1409	209957	June 9, 1998
20	DNA58848-1472	209955	June 9, 1998
	DNA58849-1494	209958	June 9, 1998
	DNA58850-1495	209956	June 9, 1998
	DNA58853-1423	203016	June 23, 1998
	DNA58855-1422	203018	June 23, 1998
25	DNA59205-1421	203009	June 23, 1998
	DNA59211-1450	209960	June 9, 1998
	DNA59213-1487	209959	June 9, 1998
	DNA59214-1449	203046	July 1, 1998
	DNA59215-1425	209961	June 9, 1998
30	DNA59220-1514	209962	June 9, 1998
	DNA59488-1603	203157	August 25, 1998
	DNA59493-1420	203050	July 1, 1998
	DNA59497-1496	209941	June 4, 1998
	DNA59588-1571	203106	August 11, 1998
35	DNA59603-1419	209944	June 9, 1998
	DNA59605-1418	203005	June 23, 1998
	DNA59606-1471	209945	June 9, 1998
	DNA59607-1497	209957	June 9, 1998
	DNA59609-1470	209963	June 9, 1998
40	DNA59610-1559	209990	June 16, 1998
	DNA59612-1466	209947	June 9, 1998
	DNA59613-1417	203007	June 23, 1998
	DNA59616-1465	209991	June 16, 1998
	DNA59619-1464	203041	July 1, 1998
45	DNA59620-1463	209989	June 16, 1998
	DNA59625-1498	209992	June 17, 1998
	DNA59767-1489	203108	August 11, 1998
	DNA59776-1600	203128	August 18, 1998
	DNA59777-1480	203111	August 11, 1998
50	DNA59820-1549	203129	August 18, 1998
	DNA59827-1426	203089	August 4, 1998
	DNA59828-1608	203158	August 25, 1998
	DNA59838-1462	209976	June 16, 1998
	DNA59839-1461	209988	June 16, 1998
55	DNA59841-1460	203044	July 1, 1998
	DNA59842-1502	209982	June 16, 1998

	DNA59846-1503	209978	June 16, 1998
	DNA59847-1511	203098	August 4, 1998
	DNA59848-1512	203088	August 4, 1998
	DNA59849-1504	209986	June 16, 1998
	DNA59853-1505	209985	June 16, 1998
5	DNA59854-1459	209974	June 16, 1998
	DNA60283-1484	203043	July 1, 1998
	DNA60615-1483	209980	June 16, 1998
	DNA60619-1482	209993	June 16, 1998
	DNA60621-1516	203091	August 4, 1998
10	DNA60622-1525	203090	August 4, 1998
	DNA60625-1507	209975	June 16, 1998
	DNA60627-1508	203092	August 4, 1998
	DNA60629-1481	209979	June 16, 1998
	DNA61755-1554	203112	August 11, 1998
15	DNA61873-1574	203132	August 18, 1998
	DNA62814-1521	203093	August 4, 1998
	DNA62872-1509	203100	August 4, 1998
	DNA62876-1517	203095	August 4, 1998
	DNA62881-1515	203096	August 4, 1998
20	DNA64852-1589	203127	August 18, 1998
	DNA64884-1527	203155	August 25, 1998
	DNA64890-1612	203131	August 18, 1998
	DNA65412-1523	203094	August 4, 1998
	DNA66308-1537	203159	August 25, 1998
25	DNA66309-1538	203235	September 15, 1998
	DNA67004-1614	203115	August 11, 1998
	DNA68869-1610	203164	August 25, 1998
	DNA68872-1620	203160	August 25, 1998
30	DNA71159-1617	203135	August 18, 1998

These deposit were made under the provisions of the Budapest Treaty on the International Recognition of the Deposit of Microorganisms for the Purpose of Patent Procedure and the Regulations thereunder (Budapest Treaty). This assures maintenance of a viable culture of the deposit for 30 years from the date of deposit. The deposits will be made available by ATCC under the terms of the Budapest Treaty, and subject to an agreement between Genentech, Inc. and ATCC, which assures permanent and unrestricted availability of the progeny of the culture of the deposit to the public upon issuance of the pertinent U.S. patent or upon laying open to the public of any U.S. or foreign patent application, whichever comes first, and assures availability of the progeny to one determined by the U.S. Commissioner of Patents and Trademarks to be entitled thereto according to 35 USC §122 and the Commissioner's rules pursuant thereto (including 37 CFR §1.14 with particular reference to 886 OG 638).

The assignee of the present application has agreed that if a culture of the materials on deposit should die or be lost or destroyed when cultivated under suitable conditions, the materials will be promptly replaced on notification with another of the same. Availability of the deposited material is not to be construed as a license to practice the invention in contravention of the rights granted under the authority of any government in accordance with its patent laws.

The foregoing written specification is considered to be sufficient to enable one skilled in the art to practice the invention. The present invention is not to be limited in scope by the construct deposited, since the



deposited embodiment is intended as a single illustration of certain aspects of the invention and any constructs that are functionally equivalent are within the scope of this invention. The deposit of material herein does not constitute an admission that the written description herein contained is inadequate to enable the practice of any aspect of the invention, including the best mode thereof, nor is it to be construed as limiting the scope of the claims to the specific illustrations that it represents. Indeed, various modifications of the invention in addition to those shown and described herein will become apparent to those skilled in the art from the foregoing description and fall within the scope of the appended claims.

WHAT IS CLAIMED IS:

1. Isolated nucleic acid having at least 80% sequence identity to a nucleotide sequence that encodes a polypeptide comprising an amino acid sequence selected from the group consisting of the amino acid sequence shown in Figure 2 (SEQ ID NO:2), Figure 4 (SEQ ID NO:6), Figure 6 (SEQ ID NO:8), Figure 9 (SEQ ID NO:14), Figure 12 (SEQ ID NO:20), Figure 15 (SEQ ID NO:23), Figure 18 (SEQ ID NO:28), Figure 20 (SEQ ID NO:30), Figure 23 (SEQ ID NO:33), Figure 25 (SEQ ID NO:36), Figure 27 (SEQ ID NO:41), Figure 30 (SEQ ID NO:47), Figure 32 (SEQ ID NO:52), Figure 34 (SEQ ID NO:57), Figure 36 (SEQ ID NO:62), Figure 38 (SEQ ID NO:67), Figure 41 (SEQ ID NO:73), Figure 47 (SEQ ID NO:84), Figure 49 (SEQ ID NO:95), Figure 51 (SEQ ID NO:97), Figure 53 (SEQ ID NO:99), Figure 57 (SEQ ID NO:103), Figure 64 (SEQ ID NO:113), Figure 66 (SEQ ID NO:115), Figure 68 (SEQ ID NO:117), Figure 70 (SEQ ID NO:119), Figure 72 (SEQ ID NO:124), Figure 74 (SEQ ID NO:129), Figure 76 (SEQ ID NO:135), Figure 79 (SEQ ID NO:138), Figure 83 (SEQ ID NO:146), Figure 85 (SEQ ID NO:148), Figure 88 (SEQ ID NO:151), Figure 90 (SEQ ID NO:153), Figure 93 (SEQ ID NO:156), Figure 95 (SEQ ID NO:158), Figure 97 (SEQ ID NO:160), Figure 99 (SEQ ID NO:165), Figure 101 (SEQ ID NO:167), Figure 103 (SEQ ID NO:169), Figure 105 (SEQ ID NO:171), Figure 109 (SEQ ID NO:175), Figure 111 (SEQ ID NO:177), Figure 113 (SEQ ID NO:179), Figure 115 (SEQ ID NO:181), Figure 117 (SEQ ID NO:183), Figure 120 (SEQ ID NO:189), Figure 122 (SEQ ID NO:194), Figure 125 (SEQ ID NO:197), Figure 127 (SEQ ID NO:199), Figure 129 (SEQ ID NO:201), Figure 131 (SEQ ID NO:203), Figure 133 (SEQ ID NO:205), Figure 135 (SEQ ID NO:207), Figure 137 (SEQ ID NO:209), Figure 139 (SEQ ID NO:211), Figure 141 (SEQ ID NO:213), Figure 144 (SEQ ID NO:216), Figure 147 (SEQ ID NO:219), Figure 149 (SEQ ID NO:221), Figure 151 (SEQ ID NO:223), Figure 153 (SEQ ID NO:225), Figure 155 (SEQ ID NO:227), Figure 157 (SEQ ID NO:229), Figure 159 (SEQ ID NO:231), Figure 161 (SEQ ID NO:236), Figure 163 (SEQ ID NO:241), Figure 165 (SEQ ID NO:246), Figure 167 (SEQ ID NO:248), Figure 169 (SEQ ID NO:250), Figure 171 (SEQ ID NO:253), Figure 174 (SEQ ID NO:256), Figure 176 (SEQ ID NO:258), Figure 178 (SEQ ID NO:260), Figure 180 (SEQ ID NO:262), Figure 182 (SEQ ID NO:264), Figure 184 (SEQ ID NO:266), Figure 186 (SEQ ID NO:268), Figure 188 (SEQ ID NO:270), Figure 190 (SEQ ID NO:272), Figure 192 (SEQ ID NO:274), Figure 194 (SEQ ID NO:276), Figure 196 (SEQ ID NO:278), Figure 198 (SEQ ID NO:281), Figure 200 (SEQ ID NO:283), Figure 202 (SEQ ID NO:285), Figure 204 (SEQ ID NO:287), Figure 206 (SEQ ID NO:289), Figure 208 (SEQ ID NO:291), Figure 210 (SEQ ID NO:293), Figure 212 (SEQ ID NO:295), Figure 214 (SEQ ID NO:297), Figure 216 (SEQ ID NO:299), Figure 218 (SEQ ID NO:301), Figure 220 (SEQ ID NO:303), Figure 226 (SEQ ID NO:309), Figure 228 (SEQ ID NO:314), Figure 230 (SEQ ID NO:319), Figure 233 (SEQ ID NO:326), Figure 235 (SEQ ID NO:334), Figure 238 (SEQ ID NO:340), Figure 240 (SEQ ID NO:345), Figure 242 (SEQ ID NO:347), Figure 244 (SEQ ID NO:349), Figure 246 (SEQ ID NO:351), Figure 248 (SEQ ID NO:353), Figure 250 (SEQ ID NO:355), Figure 252 (SEQ ID NO:357), Figure 254 (SEQ ID NO:359), Figure 256 (SEQ ID NO:361), Figure 258 (SEQ ID NO:363), Figure 260 (SEQ ID NO:365), Figure 262 (SEQ ID NO:367), Figure 264 (SEQ ID NO:369), Figure 266 (SEQ ID NO:371), Figure 268 (SEQ ID NO:373), Figure 270 (SEQ ID NO:375), Figure 272 (SEQ ID NO:377), Figure 274 (SEQ ID NO:379), Figure 276 (SEQ ID NO:381), Figure 278 (SEQ ID NO:387), Figure 280 (SEQ ID NO:389), Figure 282 (SEQ ID NO:394), Figure 284 (SEQ ID NO:399), Figure 286 (SEQ

ID NO:401), Figure 288 (SEQ ID NO:403), Figure 290 (SEQ ID NO:408), Figure 292 (SEQ ID NO:410), Figure 294 (SEQ ID NO:412), Figure 296 (SEQ ID NO:414), Figure 298 (SEQ ID NO:416), Figure 300 (SEQ ID NO:418), Figure 302 (SEQ ID NO:420), Figure 304 (SEQ ID NO:422) and Figure 306 (SEQ ID NO:424).

2. The nucleic acid sequence of Claim 1, wherein said nucleotide sequence comprises a nucleotide
- 5 sequence selected from the group consisting of the sequence shown in Figure 1 (SEQ ID NO:1), Figure 3 (SEQ ID NO:5), Figure 5 (SEQ ID NO:7), Figure 8 (SEQ ID NO:13), Figure 11 (SEQ ID NO:19), Figure 14 (SEQ ID NO:22), Figure 17 (SEQ ID NO:27), Figure 19 (SEQ ID NO:29), Figure 22 (SEQ ID NO:32), Figure 24 (SEQ ID NO:35), Figure 26 (SEQ ID NO:40), Figure 29 (SEQ ID NO:46), Figure 31 (SEQ ID NO:51), Figure 33 (SEQ ID NO:56), Figure 35 (SEQ ID NO:61), Figure 37 (SEQ ID NO:66), Figure 40 (SEQ ID NO:72),
- 10 Figure 46 (SEQ ID NO:83), Figure 48 (SEQ ID NO:94), Figure 50 (SEQ ID NO:96), Figure 52 (SEQ ID NO:98), Figure 56 (SEQ ID NO:102), Figure 63 (SEQ ID NO:112), Figure 65 (SEQ ID NO:114), Figure 67 (SEQ ID NO:116), Figure 69 (SEQ ID NO:118), Figure 71 (SEQ ID NO:123), Figure 73 (SEQ ID NO:128), Figure 75 (SEQ ID NO:134), Figure 78 (SEQ ID NO:137), Figure 82 (SEQ ID NO:145), Figure 84 (SEQ ID NO:147), Figure 87 (SEQ ID NO:150), Figure 89 (SEQ ID NO:152), Figure 92 (SEQ ID NO:155), Figure 94 (SEQ ID NO:157), Figure 96 (SEQ ID NO:159), Figure 98 (SEQ ID NO:164), Figure 100 (SEQ ID NO:166),
- 15 Figure 102 (SEQ ID NO:168), Figure 104 (SEQ ID NO:170), Figure 108 (SEQ ID NO:174), Figure 110 (SEQ ID NO:176), Figure 112 (SEQ ID NO:178), Figure 114 (SEQ ID NO:180), Figure 116 (SEQ ID NO:182), Figure 119 (SEQ ID NO:188), Figure 121 (SEQ ID NO:193), Figure 124 (SEQ ID NO:196), Figure 126 (SEQ ID NO:198), Figure 128 (SEQ ID NO:200), Figure 130 (SEQ ID NO:202), Figure 132 (SEQ ID NO:204),
- 20 Figure 134 (SEQ ID NO:206), Figure 136 (SEQ ID NO:208), Figure 138 (SEQ ID NO:210), Figure 140 (SEQ ID NO:212), Figure 143 (SEQ ID NO:215), Figure 146 (SEQ ID NO:218), Figure 148 (SEQ ID NO:220), Figure 150 (SEQ ID NO:222), Figure 152 (SEQ ID NO:224), Figure 154 (SEQ ID NO:226), Figure 156 (SEQ ID NO:228), Figure 158 (SEQ ID NO:230), Figure 160 (SEQ ID NO:235), Figure 162 (SEQ ID NO:240), Figure 164 (SEQ ID NO:245), Figure 166 (SEQ ID NO:247), Figure 168 (SEQ ID NO:249), Figure 170 (SEQ ID NO:252), Figure 173 (SEQ ID NO:255), Figure 175 (SEQ ID NO:257), Figure 177 (SEQ ID NO:259),
- 25 Figure 179 (SEQ ID NO:261), Figure 181 (SEQ ID NO:263), Figure 183 (SEQ ID NO:265), Figure 185 (SEQ ID NO:267), Figure 187 (SEQ ID NO:269), Figure 189 (SEQ ID NO:271), Figure 191 (SEQ ID NO:273), Figure 193 (SEQ ID NO:275), Figure 195 (SEQ ID NO:277), Figure 197 (SEQ ID NO:280), Figure 199 (SEQ ID NO:282), Figure 201 (SEQ ID NO:284), Figure 203 (SEQ ID NO:286), Figure 205 (SEQ ID NO:288),
- 30 Figure 207 (SEQ ID NO:290), Figure 209 (SEQ ID NO:292), Figure 211 (SEQ ID NO:294), Figure 213 (SEQ ID NO:296), Figure 215 (SEQ ID NO:298), Figure 217 (SEQ ID NO:300), Figure 219 (SEQ ID NO:302), Figure 225 (SEQ ID NO:308), Figure 227 (SEQ ID NO:313), Figure 229 (SEQ ID NO:318), Figure 232 (SEQ ID NO:325), Figure 234 (SEQ ID NO:333), Figure 237 (SEQ ID NO:339), Figure 239 (SEQ ID NO:344), Figure 241 (SEQ ID NO:346), Figure 243 (SEQ ID NO:348), Figure 245 (SEQ ID NO:350), Figure 247 (SEQ ID NO:352), Figure 249 (SEQ ID NO:354), Figure 251 (SEQ ID NO:356), Figure 253 (SEQ ID NO:358),
- 35 Figure 255 (SEQ ID NO:360), Figure 257 (SEQ ID NO:362), Figure 259 (SEQ ID NO:364), Figure 261 (SEQ ID NO:366), Figure 263 (SEQ ID NO:368), Figure 265 (SEQ ID NO:370), Figure 267 (SEQ ID NO:372),

Figure 269 (SEQ ID NO:374), Figure 271 (SEQ ID NO:376), Figure 273 (SEQ ID NO:378), Figure 275 (SEQ ID NO:380), Figure 277 (SEQ ID NO:386), Figure 279 (SEQ ID NO:388), Figure 281 (SEQ ID NO:393), Figure 283 (SEQ ID NO:398), Figure 285 (SEQ ID NO:400), Figure 287 (SEQ ID NO:402), Figure 289 (SEQ ID NO:407), Figure 291 (SEQ ID NO:409), Figure 293 (SEQ ID NO:411), Figure 295 (SEQ ID NO:413), Figure 297 (SEQ ID NO:415), Figure 299 (SEQ ID NO:417), Figure 301 (SEQ ID NO:419), Figure 303 (SEQ ID NO:421) and Figure 305 (SEQ ID NO:423).

3. The nucleic acid of Claim 1, wherein said nucleotide sequence comprises a nucleotide sequence selected from the group consisting of the full-length coding sequence of the sequence shown in Figure 1 (SEQ ID NO:1), Figure 3 (SEQ ID NO:5), Figure 5 (SEQ ID NO:7), Figure 8 (SEQ ID NO:13), Figure 11 (SEQ ID NO:19), Figure 14 (SEQ ID NO:22), Figure 17 (SEQ ID NO:27), Figure 19 (SEQ ID NO:29), Figure 22 (SEQ ID NO:32), Figure 24 (SEQ ID NO:35), Figure 26 (SEQ ID NO:40), Figure 29 (SEQ ID NO:46), Figure 31 (SEQ ID NO:51), Figure 33 (SEQ ID NO:56), Figure 35 (SEQ ID NO:61), Figure 37 (SEQ ID NO:66), Figure 40 (SEQ ID NO:72), Figure 46 (SEQ ID NO:83), Figure 48 (SEQ ID NO:94), Figure 50 (SEQ ID NO:96), Figure 52 (SEQ ID NO:98), Figure 56 (SEQ ID NO:102), Figure 63 (SEQ ID NO:112), Figure 65 (SEQ ID NO:114), Figure 67 (SEQ ID NO:116), Figure 69 (SEQ ID NO:118), Figure 71 (SEQ ID NO:123), Figure 73 (SEQ ID NO:128), Figure 75 (SEQ ID NO:134), Figure 78 (SEQ ID NO:137), Figure 82 (SEQ ID NO:145), Figure 84 (SEQ ID NO:147), Figure 87 (SEQ ID NO:150), Figure 89 (SEQ ID NO:152), Figure 92 (SEQ ID NO:155), Figure 94 (SEQ ID NO:157), Figure 96 (SEQ ID NO:159), Figure 98 (SEQ ID NO:164), Figure 100 (SEQ ID NO:166), Figure 102 (SEQ ID NO:168), Figure 104 (SEQ ID NO:170), Figure 108 (SEQ ID NO:174), Figure 110 (SEQ ID NO:176), Figure 112 (SEQ ID NO:178), Figure 114 (SEQ ID NO:180), Figure 116 (SEQ ID NO:182), Figure 119 (SEQ ID NO:188), Figure 121 (SEQ ID NO:193), Figure 124 (SEQ ID NO:196), Figure 126 (SEQ ID NO:198), Figure 128 (SEQ ID NO:200), Figure 130 (SEQ ID NO:202), Figure 132 (SEQ ID NO:204), Figure 134 (SEQ ID NO:206), Figure 136 (SEQ ID NO:208), Figure 138 (SEQ ID NO:210), Figure 140 (SEQ ID NO:212), Figure 143 (SEQ ID NO:215), Figure 146 (SEQ ID NO:218), Figure 148 (SEQ ID NO:220), Figure 150 (SEQ ID NO:222), Figure 152 (SEQ ID NO:224), Figure 154 (SEQ ID NO:226), Figure 156 (SEQ ID NO:228), Figure 158 (SEQ ID NO:230), Figure 160 (SEQ ID NO:235), Figure 162 (SEQ ID NO:240), Figure 164 (SEQ ID NO:245), Figure 166 (SEQ ID NO:247), Figure 168 (SEQ ID NO:249), Figure 170 (SEQ ID NO:252), Figure 173 (SEQ ID NO:255), Figure 175 (SEQ ID NO:257), Figure 177 (SEQ ID NO:259), Figure 179 (SEQ ID NO:261), Figure 181 (SEQ ID NO:263), Figure 183 (SEQ ID NO:265), Figure 185 (SEQ ID NO:267), Figure 187 (SEQ ID NO:269), Figure 189 (SEQ ID NO:271), Figure 191 (SEQ ID NO:273), Figure 193 (SEQ ID NO:275), Figure 195 (SEQ ID NO:277), Figure 197 (SEQ ID NO:280), Figure 199 (SEQ ID NO:282), Figure 201 (SEQ ID NO:284), Figure 203 (SEQ ID NO:286), Figure 205 (SEQ ID NO:288), Figure 207 (SEQ ID NO:290), Figure 209 (SEQ ID NO:292), Figure 211 (SEQ ID NO:294), Figure 213 (SEQ ID NO:296), Figure 215 (SEQ ID NO:298), Figure 217 (SEQ ID NO:300), Figure 219 (SEQ ID NO:302), Figure 225 (SEQ ID NO:308), Figure 227 (SEQ ID NO:313), Figure 229 (SEQ ID NO:318), Figure 232 (SEQ ID NO:325), Figure 234 (SEQ ID NO:333), Figure 237 (SEQ ID NO:339), Figure 239 (SEQ ID NO:344), Figure 241 (SEQ ID NO:346), Figure 243 (SEQ ID NO:348), Figure 245 (SEQ ID

- NO:350), Figure 247 (SEQ ID NO:352), Figure 249 (SEQ ID NO:354), Figure 251 (SEQ ID NO:356), Figure 253 (SEQ ID NO:358), Figure 255 (SEQ ID NO:360), Figure 257 (SEQ ID NO:362), Figure 259 (SEQ ID NO:364), Figure 261 (SEQ ID NO:366), Figure 263 (SEQ ID NO:368), Figure 265 (SEQ ID NO:370), Figure 267 (SEQ ID NO:372), Figure 269 (SEQ ID NO:374), Figure 271 (SEQ ID NO:376), Figure 273 (SEQ ID NO:378), Figure 275 (SEQ ID NO:380), Figure 277 (SEQ ID NO:386), Figure 279 (SEQ ID NO:388), Figure 281 (SEQ ID NO:393), Figure 283 (SEQ ID NO:398), Figure 285 (SEQ ID NO:400), Figure 287 (SEQ ID NO:402), Figure 289 (SEQ ID NO:407), Figure 291 (SEQ ID NO:409), Figure 293 (SEQ ID NO:411), Figure 295 (SEQ ID NO:413), Figure 297 (SEQ ID NO:415), Figure 299 (SEQ ID NO:417), Figure 301 (SEQ ID NO:419), Figure 303 (SEQ ID NO:421) or Figure 305 (SEQ ID NO:423).
4. Isolated nucleic acid which comprises the full-length coding sequence of the DNA deposited under any ATCC accession number shown in Table 2.
5. A vector comprising the nucleic acid of Claim 1.
6. The vector of Claim 5 operably linked to control sequences recognized by a host cell transformed with the vector.
7. A host cell comprising the vector of Claim 5.
8. The host cell of Claim 7 wherein said cell is a CHO cell.
9. The host cell of Claim 7 wherein said cell is an *E. coli*.
10. The host cell of Claim 7 wherein said cell is a yeast cell.
11. A process for producing a PRO polypeptides comprising culturing the host cell of Claim 7 under conditions suitable for expression of said PRO polypeptide and recovering said PRO polypeptide from the cell culture.
12. Isolated PRO polypeptide having at least 80% sequence identity to an amino acid sequence selected from the group consisting of the amino acid sequence shown in Figure 2 (SEQ ID NO:2), Figure 4 (SEQ ID NO:6), Figure 6 (SEQ ID NO:8), Figure 9 (SEQ ID NO:14), Figure 12 (SEQ ID NO:20), Figure 15 (SEQ ID NO:23), Figure 18 (SEQ ID NO:28), Figure 20 (SEQ ID NO:30), Figure 23 (SEQ ID NO:33), Figure 25 (SEQ ID NO:36), Figure 27 (SEQ ID NO:41), Figure 30 (SEQ ID NO:47), Figure 32 (SEQ ID NO:52), Figure 34 (SEQ ID NO:57), Figure 36 (SEQ ID NO:62), Figure 38 (SEQ ID NO:67), Figure 41 (SEQ ID NO:73), Figure 47 (SEQ ID NO:84), Figure 49 (SEQ ID NO:95), Figure 51 (SEQ ID NO:97), Figure 53 (SEQ ID NO:99), Figure 57 (SEQ ID NO:103), Figure 64 (SEQ ID NO:113), Figure 66 (SEQ ID NO:115), Figure 68

(SEQ ID NO:117), Figure 70 (SEQ ID NO:119), Figure 72 (SEQ ID NO:124), Figure 74 (SEQ ID NO:129), Figure 76 (SEQ ID NO:135), Figure 79 (SEQ ID NO:138), Figure 83 (SEQ ID NO:146), Figure 85 (SEQ ID NO:148), Figure 88 (SEQ ID NO:151), Figure 90 (SEQ ID NO:153), Figure 93 (SEQ ID NO:156), Figure 95 (SEQ ID NO:158), Figure 97 (SEQ ID NO:160), Figure 99 (SEQ ID NO:165), Figure 101 (SEQ ID NO:167), Figure 103 (SEQ ID NO:169), Figure 105 (SEQ ID NO:171), Figure 109 (SEQ ID NO:175), Figure 111 (SEQ ID NO:177), Figure 113 (SEQ ID NO:179), Figure 115 (SEQ ID NO:181), Figure 117 (SEQ ID NO:183), Figure 120 (SEQ ID NO:189), Figure 122 (SEQ ID NO:194), Figure 125 (SEQ ID NO:197), Figure 127 (SEQ ID NO:199), Figure 129 (SEQ ID NO:201), Figure 131 (SEQ ID NO:203), Figure 133 (SEQ ID NO:205), Figure 135 (SEQ ID NO:207), Figure 137 (SEQ ID NO:209), Figure 139 (SEQ ID NO:211), Figure 141 (SEQ ID NO:213), Figure 144 (SEQ ID NO:216), Figure 147 (SEQ ID NO:219), Figure 149 (SEQ ID NO:221), Figure 151 (SEQ ID NO:223), Figure 153 (SEQ ID NO:225), Figure 155 (SEQ ID NO:227), Figure 157 (SEQ ID NO:229), Figure 159 (SEQ ID NO:231), Figure 161 (SEQ ID NO:236), Figure 163 (SEQ ID NO:241), Figure 165 (SEQ ID NO:246), Figure 167 (SEQ ID NO:248), Figure 169 (SEQ ID NO:250), Figure 171 (SEQ ID NO:253), Figure 174 (SEQ ID NO:256), Figure 176 (SEQ ID NO:258), Figure 178 (SEQ ID NO:260), Figure 180 (SEQ ID NO:262), Figure 182 (SEQ ID NO:264), Figure 184 (SEQ ID NO:266), Figure 186 (SEQ ID NO:268), Figure 188 (SEQ ID NO:270), Figure 190 (SEQ ID NO:272), Figure 192 (SEQ ID NO:274), Figure 194 (SEQ ID NO:276), Figure 196 (SEQ ID NO:278), Figure 198 (SEQ ID NO:281), Figure 200 (SEQ ID NO:283), Figure 202 (SEQ ID NO:285), Figure 204 (SEQ ID NO:287), Figure 206 (SEQ ID NO:289), Figure 208 (SEQ ID NO:291), Figure 210 (SEQ ID NO:293), Figure 212 (SEQ ID NO:295), Figure 214 (SEQ ID NO:297), Figure 216 (SEQ ID NO:299), Figure 218 (SEQ ID NO:301), Figure 220 (SEQ ID NO:303), Figure 226 (SEQ ID NO:309), Figure 228 (SEQ ID NO:314), Figure 230 (SEQ ID NO:319), Figure 233 (SEQ ID NO:326), Figure 235 (SEQ ID NO:334), Figure 238 (SEQ ID NO:340), Figure 240 (SEQ ID NO:345), Figure 242 (SEQ ID NO:347), Figure 244 (SEQ ID NO:349), Figure 246 (SEQ ID NO:351), Figure 248 (SEQ ID NO:353), Figure 250 (SEQ ID NO:355), Figure 252 (SEQ ID NO:357), Figure 254 (SEQ ID NO:359), Figure 256 (SEQ ID NO:361), Figure 258 (SEQ ID NO:363), Figure 260 (SEQ ID NO:365), Figure 262 (SEQ ID NO:367), Figure 264 (SEQ ID NO:369), Figure 266 (SEQ ID NO:371), Figure 268 (SEQ ID NO:373), Figure 270 (SEQ ID NO:375), Figure 272 (SEQ ID NO:377), Figure 274 (SEQ ID NO:379), Figure 276 (SEQ ID NO:381), Figure 278 (SEQ ID NO:387), Figure 280 (SEQ ID NO:389), Figure 282 (SEQ ID NO:394), Figure 284 (SEQ ID NO:399), Figure 286 (SEQ ID NO:401), Figure 288 (SEQ ID NO:403), Figure 290 (SEQ ID NO:408), Figure 292 (SEQ ID NO:410), Figure 294 (SEQ ID NO:412), Figure 296 (SEQ ID NO:414), Figure 298 (SEQ ID NO:416), Figure 300 (SEQ ID NO:418), Figure 302 (SEQ ID NO:420), Figure 304 (SEQ ID NO:422) and Figure 306 (SEQ ID NO:424).

13. Isolated PRO polypeptide having at least 80% sequence identity to the amino acid sequence encoded by a nucleic acid molecule deposited under any ATCC accession number shown in Table 2.

14. A chimeric molecule comprising a polypeptide according to Claim 12 fused to a heterologous amino acid sequence.

15. The chimeric molecule of Claim 14 wherein said heterologous amino acid sequence is an epitope tag sequence.
16. The chimeric molecule of Claim 14 wherein said heterologous amino acid sequence is a Fc region of an immunoglobulin.
- 5 17. An antibody which specifically binds to a PRO polypeptide according to Claim 12.
18. The antibody of Claim 17 wherein said antibody is a monoclonal antibody.
- 10 19. The antibody of Claim 17 wherein said antibody is a humanized antibody.
20. The antibody of Claim 17 wherein said antibody is an antibody fragment.
21. An isolated nucleic acid molecule which has at least 80% sequence identity to a nucleic acid  
15 which comprises a nucleotide sequence selected from the group consisting of that shown in Figure 1 (SEQ ID NO:1), Figure 3 (SEQ ID NO:5), Figure 5 (SEQ ID NO:7), Figure 8 (SEQ ID NO:13), Figure 11 (SEQ ID NO:19), Figure 14 (SEQ ID NO:22), Figure 17 (SEQ ID NO:27), Figure 19 (SEQ ID NO:29), Figure 22 (SEQ ID NO:32), Figure 24 (SEQ ID NO:35), Figure 26 (SEQ ID NO:40), Figure 29 (SEQ ID NO:46), Figure 31 (SEQ ID NO:51), Figure 33 (SEQ ID NO:56), Figure 35 (SEQ ID NO:61), Figure 37 (SEQ ID NO:66), Figure  
20 40 (SEQ ID NO:72), Figure 46 (SEQ ID NO:83), Figure 48 (SEQ ID NO:94), Figure 50 (SEQ ID NO:96), Figure 52 (SEQ ID NO:98), Figure 56 (SEQ ID NO:102), Figure 63 (SEQ ID NO:112), Figure 65 (SEQ ID NO:114), Figure 67 (SEQ ID NO:116), Figure 69 (SEQ ID NO:118), Figure 71 (SEQ ID NO:123), Figure 73 (SEQ ID NO:128), Figure 75 (SEQ ID NO:134), Figure 78 (SEQ ID NO:137), Figure 82 (SEQ ID NO:145), Figure 84 (SEQ ID NO:147), Figure 87 (SEQ ID NO:150), Figure 89 (SEQ ID NO:152), Figure 92 (SEQ ID  
25 NO:155), Figure 94 (SEQ ID NO:157), Figure 96 (SEQ ID NO:159), Figure 98 (SEQ ID NO:164), Figure 100 (SEQ ID NO:166), Figure 102 (SEQ ID NO:168), Figure 104 (SEQ ID NO:170), Figure 108 (SEQ ID NO:174), Figure 110 (SEQ ID NO:176), Figure 112 (SEQ ID NO:178), Figure 114 (SEQ ID NO:180), Figure 116 (SEQ ID NO:182), Figure 119 (SEQ ID NO:188), Figure 121 (SEQ ID NO:193), Figure 124 (SEQ ID NO:196), Figure 126 (SEQ ID NO:198), Figure 128 (SEQ ID NO:200), Figure 130 (SEQ ID NO:202), Figure  
30 132 (SEQ ID NO:204), Figure 134 (SEQ ID NO:206), Figure 136 (SEQ ID NO:208), Figure 138 (SEQ ID NO:210), Figure 140 (SEQ ID NO:212), Figure 143 (SEQ ID NO:215), Figure 146 (SEQ ID NO:218), Figure 148 (SEQ ID NO:220), Figure 150 (SEQ ID NO:222), Figure 152 (SEQ ID NO:224), Figure 154 (SEQ ID NO:226), Figure 156 (SEQ ID NO:228), Figure 158 (SEQ ID NO:230), Figure 160 (SEQ ID NO:235), Figure 162 (SEQ ID NO:240), Figure 164 (SEQ ID NO:245), Figure 166 (SEQ ID NO:247), Figure 168 (SEQ ID  
35 NO:249), Figure 170 (SEQ ID NO:252), Figure 173 (SEQ ID NO:255), Figure 175 (SEQ ID NO:257), Figure 177 (SEQ ID NO:259), Figure 179 (SEQ ID NO:261), Figure 181 (SEQ ID NO:263), Figure 183 (SEQ ID NO:265), Figure 185 (SEQ ID NO:267), Figure 187 (SEQ ID NO:269), Figure 189 (SEQ ID NO:271), Figure

191 (SEQ ID NO:273), Figure 193 (SEQ ID NO:275), Figure 195 (SEQ ID NO:277), Figure 197 (SEQ ID NO:280), Figure 199 (SEQ ID NO:282), Figure 201 (SEQ ID NO:284), Figure 203 (SEQ ID NO:286), Figure 205 (SEQ ID NO:288), Figure 207 (SEQ ID NO:290), Figure 209 (SEQ ID NO:292), Figure 211 (SEQ ID NO:294), Figure 213 (SEQ ID NO:296), Figure 215 (SEQ ID NO:298), Figure 217 (SEQ ID NO:300), Figure 219 (SEQ ID NO:302), Figure 225 (SEQ ID NO:308), Figure 227 (SEQ ID NO:313), Figure 229 (SEQ ID NO:318), Figure 232 (SEQ ID NO:325), Figure 234 (SEQ ID NO:333), Figure 237 (SEQ ID NO:339), Figure 239 (SEQ ID NO:344), Figure 241 (SEQ ID NO:346), Figure 243 (SEQ ID NO:348), Figure 245 (SEQ ID NO:350), Figure 247 (SEQ ID NO:352), Figure 249 (SEQ ID NO:354), Figure 251 (SEQ ID NO:356), Figure 253 (SEQ ID NO:358), Figure 255 (SEQ ID NO:360), Figure 257 (SEQ ID NO:362), Figure 259 (SEQ ID NO:364), Figure 261 (SEQ ID NO:366), Figure 263 (SEQ ID NO:368), Figure 265 (SEQ ID NO:370), Figure 267 (SEQ ID NO:372), Figure 269 (SEQ ID NO:374), Figure 271 (SEQ ID NO:376), Figure 273 (SEQ ID NO:378), Figure 275 (SEQ ID NO:380), Figure 277 (SEQ ID NO:386), Figure 279 (SEQ ID NO:388), Figure 281 (SEQ ID NO:393), Figure 283 (SEQ ID NO:398), Figure 285 (SEQ ID NO:400), Figure 287 (SEQ ID NO:402), Figure 289 (SEQ ID NO:407), Figure 291 (SEQ ID NO:409), Figure 293 (SEQ ID NO:411), Figure 295 (SEQ ID NO:413), Figure 297 (SEQ ID NO:415), Figure 299 (SEQ ID NO:417), Figure 301 (SEQ ID NO:419), Figure 303 (SEQ ID NO:421) and Figure 305 (SEQ ID NO:423).

22. An isolated nucleic acid molecule which has at least 80% sequence identity to the full-length coding sequence of a nucleotide sequence selected from the group consisting of that shown in Figure 1 (SEQ ID NO:1), Figure 3 (SEQ ID NO:5), Figure 5 (SEQ ID NO:7), Figure 8 (SEQ ID NO:13), Figure 11 (SEQ ID NO:19), Figure 14 (SEQ ID NO:22), Figure 17 (SEQ ID NO:27), Figure 19 (SEQ ID NO:29), Figure 22 (SEQ ID NO:32), Figure 24 (SEQ ID NO:35), Figure 26 (SEQ ID NO:40), Figure 29 (SEQ ID NO:46), Figure 31 (SEQ ID NO:51), Figure 33 (SEQ ID NO:56), Figure 35 (SEQ ID NO:61), Figure 37 (SEQ ID NO:66), Figure 40 (SEQ ID NO:72), Figure 46 (SEQ ID NO:83), Figure 48 (SEQ ID NO:94), Figure 50 (SEQ ID NO:96), Figure 52 (SEQ ID NO:98), Figure 56 (SEQ ID NO:102), Figure 63 (SEQ ID NO:112), Figure 65 (SEQ ID NO:114), Figure 67 (SEQ ID NO:116), Figure 69 (SEQ ID NO:118), Figure 71 (SEQ ID NO:123), Figure 73 (SEQ ID NO:128), Figure 75 (SEQ ID NO:134), Figure 78 (SEQ ID NO:137), Figure 82 (SEQ ID NO:145), Figure 84 (SEQ ID NO:147), Figure 87 (SEQ ID NO:150), Figure 89 (SEQ ID NO:152), Figure 92 (SEQ ID NO:155), Figure 94 (SEQ ID NO:157), Figure 96 (SEQ ID NO:159), Figure 98 (SEQ ID NO:164), Figure 100 (SEQ ID NO:166), Figure 102 (SEQ ID NO:168), Figure 104 (SEQ ID NO:170), Figure 108 (SEQ ID NO:174), Figure 110 (SEQ ID NO:176), Figure 112 (SEQ ID NO:178), Figure 114 (SEQ ID NO:180), Figure 116 (SEQ ID NO:182), Figure 119 (SEQ ID NO:188), Figure 121 (SEQ ID NO:193), Figure 124 (SEQ ID NO:196), Figure 126 (SEQ ID NO:198), Figure 128 (SEQ ID NO:200), Figure 130 (SEQ ID NO:202), Figure 132 (SEQ ID NO:204), Figure 134 (SEQ ID NO:206), Figure 136 (SEQ ID NO:208), Figure 138 (SEQ ID NO:210), Figure 140 (SEQ ID NO:212), Figure 143 (SEQ ID NO:215), Figure 146 (SEQ ID NO:218), Figure 148 (SEQ ID NO:220), Figure 150 (SEQ ID NO:222), Figure 152 (SEQ ID NO:224), Figure 154 (SEQ ID NO:226), Figure 156 (SEQ ID NO:228), Figure 158 (SEQ ID NO:230), Figure 160 (SEQ ID NO:235), Figure 162 (SEQ ID NO:240), Figure 164 (SEQ ID NO:245), Figure 166 (SEQ ID NO:247), Figure 168 (SEQ ID



- NO:249), Figure 170 (SEQ ID NO:252), Figure 173 (SEQ ID NO:255), Figure 175 (SEQ ID NO:257), Figure 177 (SEQ ID NO:259), Figure 179 (SEQ ID NO:261), Figure 181 (SEQ ID NO:263), Figure 183 (SEQ ID NO:265), Figure 185 (SEQ ID NO:267), Figure 187 (SEQ ID NO:269), Figure 189 (SEQ ID NO:271), Figure 191 (SEQ ID NO:273), Figure 193 (SEQ ID NO:275), Figure 195 (SEQ ID NO:277), Figure 197 (SEQ ID NO:280), Figure 199 (SEQ ID NO:282), Figure 201 (SEQ ID NO:284), Figure 203 (SEQ ID NO:286), Figure 205 (SEQ ID NO:288), Figure 207 (SEQ ID NO:290), Figure 209 (SEQ ID NO:292), Figure 211 (SEQ ID NO:294), Figure 213 (SEQ ID NO:296), Figure 215 (SEQ ID NO:298), Figure 217 (SEQ ID NO:300), Figure 219 (SEQ ID NO:302), Figure 225 (SEQ ID NO:308), Figure 227 (SEQ ID NO:313), Figure 229 (SEQ ID NO:318), Figure 232 (SEQ ID NO:325), Figure 234 (SEQ ID NO:333), Figure 237 (SEQ ID NO:339), Figure 239 (SEQ ID NO:344), Figure 241 (SEQ ID NO:346), Figure 243 (SEQ ID NO:348), Figure 245 (SEQ ID NO:350), Figure 247 (SEQ ID NO:352), Figure 249 (SEQ ID NO:354), Figure 251 (SEQ ID NO:356), Figure 253 (SEQ ID NO:358), Figure 255 (SEQ ID NO:360), Figure 257 (SEQ ID NO:362), Figure 259 (SEQ ID NO:364), Figure 261 (SEQ ID NO:366), Figure 263 (SEQ ID NO:368), Figure 265 (SEQ ID NO:370), Figure 267 (SEQ ID NO:372), Figure 269 (SEQ ID NO:374), Figure 271 (SEQ ID NO:376), Figure 273 (SEQ ID NO:378), Figure 275 (SEQ ID NO:380), Figure 277 (SEQ ID NO:386), Figure 279 (SEQ ID NO:388), Figure 281 (SEQ ID NO:393), Figure 283 (SEQ ID NO:398), Figure 285 (SEQ ID NO:400), Figure 287 (SEQ ID NO:402), Figure 289 (SEQ ID NO:407), Figure 291 (SEQ ID NO:409), Figure 293 (SEQ ID NO:411), Figure 295 (SEQ ID NO:413), Figure 297 (SEQ ID NO:415), Figure 299 (SEQ ID NO:417), Figure 301 (SEQ ID NO:419), Figure 303 (SEQ ID NO:421) and Figure 305 (SEQ ID NO:423).
- 20           23.     An isolated extracellular domain of of PRO polypeptide.
24.     An isolated PRO polypeptide lacking its associated signal peptide.
25.     An isolated polypeptide having at least about 80% amino acid sequence identity to an  
25   extracellular domain of of PRO polypeptide.
26.     An isolated polypeptide having at least about 80% amino acid sequence identity to a PRO  
polypeptide lacking its associated signal peptide.

FIGURE 1

CGGACGCGTGGGTGCGAGGCGAAGGTGACCGGGGACCGAGCATTTAGATCTGCTCGGTAGA  
CCTGGTGCACCACCACCATGTTGGCTGCAAGGCTGGTGTGTCTCCGGACACTACCTTCTAGG  
GTTTTCCACCCAGCTTTACCAAGGCCTCCCCTGTTGTGAAGAATTCCATCACGAAGAATCA  
ATGGCTGTAAACACCTAGCAGGGAATATGCCACCAAAACAAGAATTGGGATCCGGCGTGGGA  
GAACTGGCCAAGAACTCAAAGAGGCAGCATTGGAACCATCGATGGAAAAAATATTTAAAATT  
GATCAGATGGGAAGATGGTTTGTGTGCTGGAGGGGCTGCTGTTGGTCTTGGAGCATTGTGCTA  
CTATGGCTTGGGACTGTCTAATGAGATTGGAGCTATTGAAAAGGCTGTAATTTGGCCTCAGT  
ATGTCAAGGATAGAATTCATTCCACCTATATGTACTTAGCAGGGAGTATTGGTTTAAACAGCT  
TTGTCTGCCATAGCAATCAGCAGAACGCCTGTTCTCATGAACTTCATGATGAGAGGCTCTTG  
GGTGACAATTGGTGTGACCTTTGCAGCCATGGTTGGAGCTGGAATGCTGGTACGATCAATAC  
CATATGACCAGAGCCCAGGCCCAAAGCATCTTGCTTGGTTGCTACATTCTGGTGTGATGGGT  
GCAGTGGTGGCTCCTCTGACAATATTAGGGGGTCTCTTCTCATCAGAGCTGCATGGTACAC  
AGCTGGCATTGTGGGAGGCCTCTCCACTGTGGCCATGTGTGCGCCAGTGAAAAGTTTCTGA  
ACATGGGTGCACCCCTGGGAGTGGGCCTGGGTCTCGTCTTTGTGTCCTCATTGGGATCTATG  
TTTCTTCCACCTACCACCGTGGCTGGTGCCACTCTTTACTCAGTGGCAATGTACGGTGGATT  
AGTTCTTTTTCAGCATGTTTCTTCTGTATGATACCCAGAAAGTAATCAAGCGTGCAGAAGTAT  
CACCAATGTATGGAGTTCAAAAATATGATCCCATTAACCTCGATGCTGAGTATCTACATGGAT  
ACATTAAATATATTTATGCGAGTTGCAACTATGCTGGCAACTGGAGGCAACAGAAAGAAATG  
AAGTGACTCAGCTTCTGGCTTCTCTGCTACATCAAATATCTTGTTTAATGGGGCAGATATGC  
ATTAAATAGTTTGTACAAGCAGCTTTCTGTTGAAGTTTAGAAGATAAGAAACATGTCATCATA  
TTTAAATGTTCCGGTAATGTGATGCCTCAGGTCTGCCTTTTTTTCTGGAGAATAAATGCAGT  
AATCCTCTCCCAAATAAGCACACACATTTTCAATTCTCATGTTTGAGTGATTTTAAAATGTT  
TTGGTGAATGTGAAAACATAAGTTTGTGTGATGAGAATGTAAGTCTTTTTTCTACTTTAAAA  
TTTAGTAGGTTCACTGAGTAACATAAAATTTAGCAAACCTGTGTTTGATATTTTTTTGGAGT  
GCAGAATATTGTAATTAATGTCATAAGTGATTTGGAGCTTTGGTAAAGGGACCAGAGAGAAG  
GAGTCACCTGCAGTCTTTTGTGTTTTTAAATACTTAGAACCTTAGCACTTGTGTTATTGATTA  
GTGAGGAGCCAGTAAGAAACATCTGGGTATTTGGAAACAAGTGGTCATTGTTACATTCATTT  
GCTGAACTTAACAAAACCTGTTTCATCCTGAAACAGGCACAGGTGATGCATTCTCCTGCTGTTG  
CTTCTCAGTGCTCTCTTTCCAATATAGATGTGGTCACTGTTTGACTTGTACAGAATGTTAATC  
ATACAGAGAATCCTTGATGGAATTATATATGTGTGTTTTACTTTTGAATGTTACAAAAGGAA  
ATAACTTTAAAACATTCTCAAGAGAAAATATTCAAAGCATGAAATATGTTGCTTTTTCCAG  
AATACAAACAGTATACTCATG

FIGURE 2

MLAARLVCLRTLPSRVFHPAFTKASPVVKNSITKNQWLLTPSREYATKTRIGIRRGRTGQEL  
KEAALEPSMEKIFKIDQMGRWVFVAGGAAVGLGALCYGLGLSNEIGAIEKAVIWPQYVKDRI  
HSTMYLAGSIGLTALSAIAISRTPVLMNFMMRGSWVTIGVTFAAMVGAGMLVRSIPYDQSP  
GPKHLAWLLHSGVMGAVVAPLTIILGGPLLIRAAWYTAGIVGGLSTVAMCAPSEKFLNMGAPL  
GVGLGLVFVSSLGSMFLPPTTVAGATLYSVAMYGGLVLFMSMFLLYDTQKVIKRAEVSPMYGV  
QKYDPINSMLSIYMDTLNIFMRVATMLATGGRKK

FIGURE 3

GAAGGCTGCCTCGCTGGTCCGAATTCCGGTGGCGCCACGTCCGCCCGTCTCCGCCTTCTGCAT  
CGCGGCTTCGGCGGCTTCCACCTAGACACCTAACAGTCCGCGAGCCCGCCGCGTCTGAGGG  
GGTCCGCACGGGAGTCCGGCGGTCTTGTGCATCTTGGCTACCTGTGGGTCCAAGATGTCGG  
ACATCGGAGACTGGTTCAGGAGCATCCCGCGCATCACGCGCTATTGGTTCGCGCCACCGTC  
GCCGTGCCCTTGGTCCGCAAACTCGGCCTCATCAGCCCGGCTACCTCTTCTCTGGCCCCGA  
AGCCTTCTTTATCGCTTTCAGATTTGGAGGCCAATCACTGCCACCTTTTATTTCCCTGTGG  
GTCCAGGAACCTGGATTTCTTTATTTGGTCAATTTATATTTCTTATATCAGTATTTCTACGCGA  
CTTGAAACAGGAGCTTTTGATGGGAGGCCAGCAGACTATTTATTCATGCTCCTCTTTAACTG  
GATTTGCATCGTGATTACTGGCTTAGCAATGGATATGCAGTTGCTGATGATTCCTCTGATCA  
TGTCAGTACTTTATGTCTGGGCCCAGCTGAACAGAGACATGATTGTATCATTTTGGTTTGGGA  
ACACGATTTAAGGCCTGCTATTTACCTGGGTTATCCTTGGATTCAACTATATCATCGGAGG  
CTCGGTAATCAATGAGCTTATTGGAAATCTGGTTGGACATCTTTATTTTTCTTAATGTTCA  
GATACCCAATGGACTTGGGAGGAAGAAATTTCTATCCACACCTCAGTTTTTGTACCGCTGG  
CTGCCCAGTAGGAGAGGAGGAGTATCAGGATTTGGTGTGCCCCCTGCTAGCATGAGGCGAGC  
TGCTGATCAGAATGGCGGAGGCGGGAGACAACTGGGGCCAGGGCTTTCGACTTGGAGACC  
AGTGAAGGGGCGGCTTCGGGCAGCCGCTCCTCTCAAGCCACATTTCCCTCCAGTGTCTGGGTG  
CACTTAACAACCTGCGTTCCTGGCTAACACTGTTGGACCTGACCCACACTGAATGTAGTCTTTC  
AGTACGAGACAAAGTTTCTTAAATCCCGAAGAAAAATATAAGTGTCCACAAGTTTCACGAT  
TCTCATTCAAGTCTTACTGCTGTGAAGAACAATACCAACTGTGCAAAATGCAAACTGCAC  
TACATTTTTTGGTGTCTTCTCTTCTCCCTTTCCGTCTGAATAATGGGTTTTAGCGGGTCTT  
AATCTGCTGGCATTGAGCTGGGGCTGGGTACCAAACCTTCCCAAAAGGACCTTATCTCTT  
TCTTGACACATGCCTCTCTCCCACTTTTCCCAACCCCACTTTGCAACTAGAAAAAGTTG  
CCATAAAATTTGCTCTGCCCTTGACAGGTTCTGTTATTTATTGACTTTTGCCAAGGCTGGTC  
ACAACAATCATATTCACGTTATTTTTCCCTTTTGGTGGCAGAACTGTTACCAATAGGGGGAG  
AAGACAGCCACGGATGAAGCGTTTCTCAGCTTTTGAATGCTTCGACTGACATCCGTTGTT  
AACCCTTTGGCACTCTTCAGATATTTTTTATAAAAAAGTACCAGTGAAGTTTATGAGGGCCA  
CAGATTGGTTATTAATGAGATACGAGGGTTGGTGTCTGGGTGTTTGTTCCTGAGCTAAGTGA  
TCAAGACTGTAGTGGAGTTGCAGCTAACATGGGTTAGGTTTAAACCATGGGGGATGCACCCC  
TTTGCGTTTCATATGTAGCCCTACTGGCTTTGTGTAGCTGGAGTAGTTGGGTTGCTTTGTGT  
TAGGAGGATCCAGATCATGTTGGCTACAGGGAGATGCTCTCTTTGAGAGGTCCTGGGCATTG  
ATTCCTCATTTCAATCTCATTCTGGATATGTGTTTATTGAGTAAAGGAGGAGAGCCCTCATA  
CGCTATTTAAATGTCACTTTTTTGCCTATCCCCGTTTTTTGGTTCATGTTTCAATTAATTGT  
GAGGAAGGCGCAGCTCCTCTCTGCACGTAGATCATTTTTTAAAGCTAATGTAAGCACATCTA  
AGGGAATAACATGATTTAAGGTTGAAATGGCTTTAGAATCATTTGGGTTTGAGGGTGTGTTA  
TTTTGAGTCATGAATGTACAAGCTCTGTGAATCAGACCAGCTTAAATACCCACACCTTTTTT  
TCGTAGGTGGGCTTTTCTATCAGAGCTTGGCTCATAACCAATAAAGTTTTTTGAAGGCCA  
TGGCTTTTACACAGTTATTTTATTTTATGACGTTATCTGAAAGCAGACTGTTAGGAGCAGT  
ATTGAGTGGCTGTCACTTTTGGGCAACTAAAAAGGCTTCAAACGTTTTTGATCAGTTTCTT  
TTCAGGAAACATTGTGCTCTAACAGTATGACTATTCTTTCCCCACTCTTAAACAGTGTGAT  
GTGTGTTATCCTAGGAAATGAGAGTTGGCAAACAACCTTCTCATTTTGAATAGAGTTTGTGTG  
TACTTCTCCATATTTAATTTATATGATAAAATAGGTGGGAGAGTCTGAACCTTAACTGTCA  
TGTTTTTGTGTTTCTGTGGCCACAATAAAGTTTACTTGTAATTTTATAGAGGCCATTACT  
CCAATTATGTTGCACGTACACTCATTGTACAGGCGTGGAGACTCATTGTATGTATAAGAATA  
TTTCTGACAGTGAGTGACCCGGAGTCTCTGGTGTACCTCTTACCAGTCAGCTGCCTGCCGAG  
CAGTCATTTTTTCTAAAGGTTTACAAGTATTTAGAACTTTTCAAGTTTCAAGGCAAAATGTTT  
ATGAAGTTATTCTCTTAAACATGGTTAGGAAGCTGATGACGTTATTGATTTTGTCTGGATT  
ATGTTTCTGGAATAATTTTACCAAAACAAGCTATTTGAGTTTTGACTTGACAAGGCAAAACA  
TGACAGTGGATTCTCTTTACAAATGGAAAAAATCCTTATTTTGTATAAAGGACTTCCC  
TTTTTGTAATACTAATCCTTTTTATTGGTAAAAATGTAAATTAATAATGTGCAACTTG

FIGURE 4

MSDIGDWFRSIPAITRYWFAATVAVPLVGKLGGLISPAYLFLWPEAFLYRFQIWRPITATFYF  
PVGPGTGFLYLVLNLYFLYQYSTRLETGAFDGRPADYLFMLLFNWICIVITGLAMDMQLLMIP  
LIMSVLYVWAQLNRDMIVSFWFGTRFKACYLPWVILGFNYIIIGGSVINELIGNLVGHLYFFL  
MFRYPMDLGGRNFLSTPQFLYRWLPSRRGGVSGFGVPPASMRRAADQNGGGGRHNWGQGFRLLGDQ

FIGURE 5

GGGGCCGCGGTCTAGGGCGGCTACGTGTGTTGCCATAGCGACCATTTTGCATTAACTGGTTG  
GTAGCTTCTATCCTGGGGGCTGAGCGACTGCGGGCCAGCTCTTCCCCTACTCCCTCTCGGCT  
CCTTGTGGCCCAAAGGCCCTAACCGGGGTCCGGCGGTCTGGCCTAGGGATCTTCCCCGTTGCC  
CCTTGGGGCGGGATGGCTGCGGAAGAAGAAGACGAGGTGGAGTGGGTAGTGGAGAGCATCG  
CGGGGTTCCTGCGAGGCCAGACTGGTCCATCCCCATCTTGGACTTTGTGGAACAGAAATGT  
GAAGTTAACTGCAAAGGAGGGCATGTGATAACTCCAGGAAGCCCAGAGCCGGTGATTTTGGT  
GGCCTGTGTTCCCCTTGTTTTTGATGATGAAGAAGAAAGCAAATTGACCTATACAGAGATTG  
ATCAGGAATACAAAGAAGTAGTTGAAAAGCTGTTAGAAGGTTACCTCAAAGAAATTGGAATT  
AATGAAGATCAATTTCAAGAAGCATGCACTTCTCCTCTTGCAAAGACCCATACATCACAGGC  
CATTTTGC AACCTGTGTTGGCAGCAGAAGATTTTACTATCTTTAAAGCAATGATGGTCCAGA  
AAAACATTGAAATGCAGCTGCAAGCCATTGCAATAATTCAAGAGAGAAATGGTGTATTACCT  
GACTGCTTAACCGATGGCTCTGATGTGGTCAGTGACCTTGAACACGAAGAGATGAAAATCCT  
GAGGGAAGTTCTTAGAAAATCAAAAGAGGAATATGACCAGGAAGAAGAAAGGAAGAGGAAAA  
AACAGTTATCAGAGGCTAAAACAGAAGAGCCACAGTGCATTCCAGTGAAGCTGCAATAATG  
AATAATTCCCAAGGGGATGGTGAACATTTTGCACACCCACCCCTCAGAAGTTAAAATGCATTT  
TGCTAATCAGTCAATAGAACCTTTGGGAAGAAAAGTGGAAAGGTCTGAAACTTCCTCCCTCC  
CACAAAAGGCCTGAAGATTCTTGGCTTAGAGCATGCGAGCATTGAAGGACCAATAGCAAAC  
TTATCAGTACTTGGAACAGAAGAACTTCGGCAACGAGAACACTATCTCAAGCAGAAGAGAGA  
TAAGTTGATGTCCATGAGAAAGGATATGAGGACTAAACAGATACAAAATATGGAGCAGAAAG  
GAAAACCCACTGGGGAGGTAGAGGAAATGACAGAGAAACCAGAAATGACAGCAGAGGAGAAG  
CAAACATTACTAAAGAGGAGATTGCTTGCAGAGAAACTCAAAGAAGAAGTTATTAATAAGTA  
ATAATTAAGAACAATTTAACAAAATGGAAGTTCAAATTGTCTTAAAAATAAATTATTTAGTC  
CTTACACTG

FIGURE 6

MAAEEDEVEWVVESIAGFLRGPDWSIPILDFVEQCEVNCKGGHVITPGSPEPVILVACVP  
LVFDDEESKLTYTEIHQEYKELVEKLLEGYLKEIGINEDQFQEAactsSPLAKTHTSQAILQP  
VLAAEDFTIFKAMMVQKNIEMLQAIRIIQERNGLVPDCLTDGSDVVSdleHEEMKILREVL  
RKSKEEYDQEEERKRKKQLSEAKTEEPTVHSSEAAIMNNSQGDGEHFAHPPSEVKMHFANQS  
IEPLGRKVERSETSSLPQKGLKIPGLEHASIEGP IANLSVLGTEELRQREHYLKQKRDKLMS  
MRKDMRTKQIQNMEQKGKPTGEVEEMTEKPEMTAEEKQTLLKRRLLAeKLKEEVINK

FIGURE 7

GGGCACAGCACATGTGAAGTTTTTGATGATGAAGAAGA?AGCAAATTGACCTATACAGAGAT  
TCATCAGGAATACAAAGAACTAGTTGAAAAGCTGTTAGAAGGTTACCTCAAAGAAATTGGAA  
TTAATGAAGATCAATTTCAAGAAGCATGCACTTCTCCTCTTGCAAAGACCCATACATCACAG  
GCCATTTTTGCAACCTGTGTTGGCAGCAGAAGATTTTACTATCTTTAAAGCAATGATGGTCC  
AGAAAAACATTGAAATGCAGCTGCAAGCCATTGAATAATTCAAGAGAGAAATGGTGTATTA  
CCTGACTGCTTAACCGATGGCTCTGATGTGGTCAGTGACCTTGAACACGAAGAGATGAAAAT  
CCTGAGGGAAGTTCTTAGAAAATCAAAAAGAGGAATATGACCAGGAA



FIGURE 8

GC GTGG TTTT GTTCTG CAATAGGCGGCTTAGAGGGAGGGGCTTTTTCGCCTATACCTACTG  
TAGCTTCTCCACGTATGGACCCTAAAGGCTACTGCTGCTACTACGGGGCTAGACAGTTACTG  
TCTCAGCTCTAGGATGTGCGTTCTTCCACTAGAAGCTCTTCTGAGGGAGGTAATTA AAAAAC  
AGTGGAAATGGAAAAACAGTGCTGTAGTCATCCTGTAATATGCTCCTTGTC AACAATGTATAC  
ATTCTGCTAGGTGCCATATTCATTGCTTTAAGCTCAAGTCGCATCTTACTAGTGAAGTATT  
CTGCCAATGAAGAAAAACAAGTATGATTATCTTCCA ACTACTGTGAATGTGTGCTCAGAACTG  
GTGAAGCTAGTTTTCTGTGTGCTTGTGTCA TTCTGTGTATAAAGAAAGATCATCAAAGTAG  
AAATTTGAAATATGCTTCCTGGAAGGAATTCTCTGATTTTCATGAAGTGGTCCATTCCTGCCT  
TTCTTTATTTCTTGATAACTTGATTGTCTTCTATGTCTCTGCTATCTTCAACCAGCCATG  
GCTGTTATCTTCTCAAATTTTAGCATTATAACAACAGCTCTTCTATT CAGGATAGTGCTGAA  
GAGGCGTCTAAACTGGATCCAGTGGGCTTCCCTCCTGACTTTATTTTGTCTATTGTGGCCT  
TGACTGCCGGGACTAAACTTTACAGCACA ACTTGGCAGGACGTGGATTT CATCACGATGCC  
TTTTTCAGCCCTTCCAATTCCTGCCTTCTTTTCAGAAAGTGAGTGTCCAGAAAAGACAATTG  
TACAGCAAAGGAATGGACTTTTCTGAAGCTAAATGGAACACCACAGCCAGAGTTTT CAGTC  
ACATCCGTCTTGGCATGGGCCATGTTCTTATTATAGTCCAGTGTTTTATTCTTCAATGGCT  
AATATCTATAATGAAAAGATACTGAAGGAGGGGAACCAGCTCACTGAAAGCATCTTCATACA  
GAACAGCAA ACTCTATTTCTTGGCATTCTGTTTAATGGGCTGACTCTGGGCCTTCAGAGGA  
GTAACCGTGATCAGATTAAGAACTGTGGATTTTTTATGGCCACAGTGCA TTTTCAGTAGCC  
CTTATTTTTGTAACTGCATTCCAGGGCCTTTCAGTGGCTTTCATTCTGAAGTTCCTGGATAA  
CATGTTCCATGTCTTGATGGCCAGGTTACCACTGT CATTATCACAACAGTGTCTGTCTCTGG  
TCTTTGACTTCAGGCCCTCCCTGGAA TTTTCTTGGAAAGCCCATCAGTCCCTTCTCTCTATA  
TTTATTTATAATGCCAGCAAGCCTCAAGTTC CGGAATACGCACCTAGGCAAGAAAGGATCCG  
AGATCTAAGTGGCAATCTTTGGGAGCGTTCAGTGGGGATGGAGAAGAACTAGAAAAGACTTA  
CCAAACCC AAGAGTGATGAGTCAGATGAAGATACTTTCTAACTGGTACCCACATAGTTTGCA  
GCTCTCTTGAACCTTATTTTCACATTTTCAGTGTGTGTAATATTTATCTTTTCACTTTTGATA  
AACCAGAAATGTTTCTAAATCCTAATATTCTTTGCATATATCTAGCTACTCCCTAAAATGGTT  
CCATCCAAGGCTTAGAGTACCCAAAGGCTAAGAAAT TCTAAAGAACTGATACAGGAGTAACA  
ATATGAAGAATTCA TTAATATCTCAGTACTTGATAAATCAGAAAGTTATATGTGCAGATTAT  
TTTCTTGGCCCTTCAAGCTTCCAAAAA ACTTGTAATAATCATGTTAGCTATAGCTTGTATAT  
ACACATAGAGATCAATTTGCCAAATATT CACAATCATGTAGTTCTAGTTTACATGCCAAAGT  
CTTCCCTTTTAA CATTATAAAAGCTAGGTTGTCTCTTGAATTTTGAGGCCCTAGAGATAGT  
CATTTTGAAGTAAAGAGCAACGGGACCCTTTCTAAAAACGTTGGTTGAAGGACCTAAATAC  
CTGGCCATACCATAGATT TGGGATGATGTAGTCTGTGCTAAATATTTTGCTGAAGAAGCAGT  
TTCTCAGACACAACATCTCAGAATTTTAATTTT TAGAAATTCATGGGAAATTGGATTTTTGT  
AATAATCTTTTGATGTTTTAAACATTGGTTCCCTAGTCACCATAGTTACC ACTTGTATTTTA  
AGTCATTTAAACAAGCCACGGTGGGGCTTTTTTCTCCTCAGTTTGAGGAGAAAAATCTTGAT  
GTCATTACTCCTGAATTATTACATTTTGGAGAATAAGAGGGCATTTTATTTTATTAGTTACT  
AATTCAAGCTGTGACTATTGTATATCTTTCCAAGAGTTGAAATGCTGGCTTCAGAATCATAC  
CAGATTGT CAGTGAAGCTGATGCCTAGGAACTTTTAAAGGGATCCTTTCAAAGGATCACTT  
AGCAAACACATGTTGACTTTTAACTGATGTATGAATATTAATACTCTAAAAATAGAAAGACC  
AGTAATATATAAGTCACTTTACAGTGCTACTTCACACTTAAAAGTGCATGGTATTTTTTCATG  
GTATTTTGCATGCAGCCAGTTAACTCTCGTAGATAGAGAAGTCAGGTGATAGATGATATTAA  
AAATTAGCAAACAAAAGTGACTTGCTCAGGGTCATGCAGCTGGGTGATGATAGAAGAGTGGG  
CTTTAACTGGCAGGCCTGTATGTTTACAGACTACCATACTGTAAATATGAGCTTTATGGTGT  
CATTCTCAGAACTTATACATTTCTGCTCTCCTTTCTCCTAAGTTTCATGCAGATGAATATA  
AGGTAATATACTATTATATAATTCATTTGTGATATCCACAATAATATGACTGGCAAGAATTG  
GTGGAAATTTGTAATTAAAATAATTATTAAACCT

FIGURE 9

MEKQCCSHPVICSLSTMYTFLLGAIFIALSSSRILLVKYSANEENKYDYLPTTVNVCSELVK  
LVFCVLVSFCVIKKDHQSRNLKYASWKEFSDFMKWSIPAFLYFLDNLI VFYVLSYLQPAMAV  
IFS NFSI I TTALLFRIVLKRRLNWIQWASLLTLFLSIVALTAGTKTLQHNLAGRGFHHDAFF  
SPSNSCLLFRSECPRKDNCTAKEWTFPEAKWNTTARVFSHIRLGMGHVLIIVQCFISSMANI  
YNEKILKEGNQLTESIFIQNSKLYFFGILFNGLTLGLQRSNRDQIKNCGFFYGHSAFSVALI  
FVTAFQGLSVAFILKFLDNMFHVLMAQVTTVIITTVSVLVFDFRPSLEFFLEAPSVLLSIFI  
YNASKPQVPEYAPRQERIRDLSGNLWERSSSGDGEELERLTKPKSDESEDTF

FIGURE 10

CGTGCCTGCGCAATGGGTGTCGGGTCCGCTTTTTCCCAATCCGGACGTAATCGTGGTTTTTG  
TTCTGCAATAGGCGGCTTAGAGGGAGGGGCTTTTTCGCCTATACCTACTGTAGCTTCTCCAC  
GTATGGACCCCTAAAGGCTACTGCTGCTACTACGGGGCTAGACAGTTACTGTCTCAGCTCTAG  
GATGTGCGTTCTTCCACTAGAAGCTCTTCTGAGGGAGGTAATTAAAAACAGTGGAATGGAA  
AAACAGTGCTGTAGTCATCCTGTAATATGCTCCTTGTCAACAATGTATACATTCTGCTAGG  
TGCCATATTCATTGCTTTAAGCTCAAGTCGCATCTTACTAGTGAAGTATTCTGCCAATGAAG  
AAAACAAGTATGATTATCTTCCAACACTGTGAATGTGTGCTCAGAACTGGTGAAGCTAGTT  
TTCTGTGTGCTTGTGTCATTCTGTGTTATAAAGAAAGATCATCAAAGTAGAAATTTGAAATA  
TGCTTCCTGGAAGGAATTCTCTGATTTTCATGAAGTGGTCCATTCCTGCCTTTCTTTATTTCC  
TGGATAACTTGATTGTCTTCTATGTCCTGTCCTATCTTCAACCAGCCATGGCTGTTATCTTC  
TCAAATTTTAGCATTATAACAACAGCTCTTCTATTTCAGGATAGTGCTGAAGAGGCGTCTAAA  
CTGGATCCAGTGGGCTTCCCTCCTGACTTTATTTTTGTCTATTGTGGCCTTGAAGTCCCGGA  
CTAAACTTTA

FIGURE 11

CGGACGCGTGGGCGGACGCGTGGGCGGACGCGTGGGGCCGGCTTGGCTAGCGCGCGGCGGCC  
GTGGCTAAGGCTGCTACGAAGCGAGCTTGGGAGGAGCAGCGGCCTGCGGGGCAGAGGAGCAT  
CCCGTCTACCAGGTCCCAAGCGGCGTGGCCCGCGGGTCATGGCCAAAGGAGAAGGCGCCGAG  
AGCGGCTCCGCGGCGGGGCTGCTACCCACCAGCATCCTCCAAAGCACTGAACGCCCCGGCCCA  
GGTGAAGAAAGAACCGAAAAAGAAGAAACAACAGTTGTCTGTTGCAACAAGCTTTGCTATG  
CACTTGGGGGAGCCCCCTACCAGGTGACGGGCTGTGCCCTGGGTTTCTTCCTTCAGATCTAC  
CTATTGGATGTGGCTCAGGTGGGCCCTTTCTCTGCCTCCATCATCCTGTTTGTGGGCCGAGC  
CTGGGATGCCATCACAGACCCCTGGTGGGCCTCTGCATCAGCAAATCCCCCTGGACCTGCC  
TGGGTGCGCTTATGCCCTGGATCATCTTCTCCACGCCCCCTGGCCGTCAATTGCCTACTTCCTC  
ATCTGGTTTCGTGCCCCGACTTCCCACACGGCCAGACCTATTGGTACCTGCTTTTCTATTGCCT  
CTTTGAAACAATGGTCACGTGTTTCCATGTTCCCTACTCGGCTCTCACCATGTTTCATCAGCA  
ACCGAGCAGACTGAGCGGGATTCTGCCACCGCCTATCGGATGACTGTGGAAGTGCTGGGCAC  
AGTGCTGGGCACGGCGATCCAGGGACAAATCGTGGGCCAAGCAGACACGCCTTGTTTCCAGG  
ACTTCAATAGCTCTACAGTAGCTTCACAAAGTGCCAACCATAACATGGCACCCTTCACAC  
AGGGAAACGCAAAAGGCATACCTGCTGGCAGCGGGGTCAATTGTCTGTATCTATATAATCTG  
TGCTGTCTATCCTGATCCTGGGCGTGCGGGAGCAGAGAGAAACCCTATGAAGCCCAGCAGTCTG  
AGCCAATCGCCTACTTCCGGGGCCTACGGCTGGTCACTGAGCCACGGCCCATAACATCAAACCT  
ATTACTGGCTTCTCTTACCTCCTTGGCTTTCATGCTGGTGGAGGGAACTTTGTCTTGTT  
TTGCACCTACACCTTGGGCTTCCGCAATGAATTCCAGAATCTACTCCTGGCCATCATGCTCT  
CGGCCACTTTAACCATTCCCATCTGGCAGTGTTCTTGACCCGGTTTGGCAAGAAGACAGCT  
GTATATGTTGGGATCTCATCAGCAGTGCCATTTCTCATCTTGGTGGCCCTCATGGAGAGTAA  
CCTCATCATTACATATGCGGTAGCTGTGGCAGCTGGCATCAGTGTGGCAGCTGCCTTCTTAC  
TACCCTGGTCCATGCTGCCTGATGTCAATTGACGACTTCCATCTGAAGCAGCCCCACTTCCAT  
GGAACCGAGCCCATCTTCTTCTCCTTCTATGTCTTCTTACCAAGTTTGCTCTGGAGTGTC  
ACTGGGCATTTCTACCCCTCAGTCTGGACTTTGCAGGGTACCAGACCCGTGGCTGCTCGCAGC  
CGGAACGTGTCAAGTTTACACTGAACATGCTCGTGACCATGGCTCCCATAGTTCTCATCCTG  
CTGGGCCTGCTGCTCTTCAAATGTACCCCATTGATGAGGAGAGGCGGCGGCAGAATAAGAA  
GGCCCTGCAGGCACTGAGGGACGAGGCCAGCAGCTCTGGCTGCTCAGAAACAGACTCCACAG  
AGCTGGCTAGCATCCTCTAGGGCCCGCCACGTTGCCCCGAAGCCACCATGCAGAAGGCCACAG  
AAGGGATCAGGACCTGTCTGCCGGCTTGCTGAGCAGCTGGACTGCAGGTGCTAGGAAGGGAA  
CTGAAGACTCAAGGAGGTGGCCAGGACACTTGCTGTGCTCACTGTGGGGCCGGCTGCTCTG  
TGGCCTCCTGCCTCCCCCTCTGCCTGCCTGTGGGGCCAAGCCCTGGGGCTGCCACTGTGAATA  
TGCCAAGGACTGATCGGGCCTAGCCCGGAACACTAATGTAGAAACCTTTTTTTTACAGAGCC  
TAATTAATAACTTAATGACTGTGTACATAGCAATGTGTGTATGTATATGTCTGTGAGCTA  
TTAATGTTATTAAATTTTCATAAAAGCTGGAAAGC

FIGURE 12

MWLRWALS LPPSSCLWAEPGMPSQTPWWASA'SANPPGPAWVALCPGSSSPRPWPSLPTSSSG  
SCPTSHTARPIGTCFSIASLKQWSRVSMFPTRLSPCSSATEQTERDSATAYRMTVEVLGTVL  
GTAIQQQIVGQADTPCFQDFNSSTVASQSANHTHGTTSHRETQKAYLLAAGVIVCIYIICAV  
ILILGVREQREPYEAQQSEPIAYFRGLRLVMSHGPYIKLITGFLFTSLAFMLVEGNFVLFCT  
YTLGFRNEFQNL LLAIMLSATLTIPWQWFLTRFGKKTAVYVGISSAVPFLILVALMESNLI  
ITYAVAVAAGISVAAAFLLPWSMLPDVIDDFHLKQPHFHGTEPIFFSFYVFFTKFASGVSLG  
ISTLSLDFAGYQTRGCSQPERVKFTLNMLVTMAPIVLILLGLLLFKMYPIDEERRRQNKAL  
QALRDEASSSGCSETDSTELASIL

FIGURE 13

GGGAAACGCAAAGGCATACCTGCTGGCAGCGGGGGTCATTGTCTGTATCTATATAATCTGT  
GCTGTCATCCTGATCCTGGGCGTGCGGGAGCAGAGAGAACCCTATGAAGCCCAGCAGTCTGA  
GCCAATCGCCTACTTCCGGGGCCTACGGCTGGTCATGAGCCACGGCCCATACATCAAACCTTA  
TTACTGGCTTCCTCTTCACCTCCTTGGCTTTTCATGCTGGTGGAGGGGAACCTTGTCTTGTTT  
TGCACCTACACCTTGGGCTTCCGCAATGAATTCCAGAATCTACTCCTGGCCATCATGCTCTC  
GGCCACTTTAACCATTCCCATCTGGCAGTGGTTCTTGACCCGGTTTGGCAAGAAGACAGCTG  
TATATGTTGGGATCTCATCAGCAGTGCCATTTCTCATCTTGGTGGCCCTCATGGAGAGTAAC  
CTCATCATTACATATGCGGTAGCTGTGGCAGCTGGCATCAGTGTGGCAGCTGCCTTCTTACT  
ACCCTGGTCCATGCTGCCTGATGTCATTGACGACTTCCATCTGAAGCAGCCCCACTTCCATG  
GAACCGAGCCCAT

FIGURE 14

GGGGCTTCGGCGCCAGCGGCCAGCGCTAGTCGGTCTGGTAAGGATTTACAAAAGGTGCAGGT  
ATGAGCAGGTCTGAAGACTAACATTTTGTGAAGTTGTAAAACAGAAAACCTGTTAGAAATGT  
GGTGGTTTCAGCAAGGCCTCAGTTTCCTTCCTTCAGCCCTTGTAATTTGGACATCTGCTGCT  
TTCATATTTTCATACATTACTGCAGTAACACTCCACCATATAGACCCGGCTTTACCTTATAT  
CAGTGACACTGGTACAGTAGCTCCAGAAAAATGCTTATTTGGGGCAATGCTAAATATTGCGG  
CAGTTTTATGCATTGCTACCATTTATGTTTCGTTATAAGCAAGTTCATGCTCTGAGTCCTGAA  
GAGAACGTTATCATCAAATTAAACAAGGCTGGCCTTGTAAGTGAATACTGAGTTGTTTAGG  
ACTTCTATTGTGGCAAACCTCCAGAAAAACAACCCTTTTGTCTGCACATGTAAGTGGAGCTG  
TGCTTACCTTTGGTATGGGCTCATTATATATGTTTGTTCAGACCATCCTTTCCTACCAAATG  
CAGCCCCAAATCCATGGCAAACAAGTCTTCTGGATCAGACTGTTGTTGGTTATCTGGTGTGG  
AGTAAGTGCACTTAGCATGCTGACTTGCTCATCAGTTTTGCACAGTGGCAATTTTGGGACTG  
ATTTAGAACAGAACTCCATTGGAACCCCGAGGACAAAGGTTATGTGCTTCACATGATCACT  
ACTGCAGCAGAATGGTCTATGTCATTTTCCTTCTTTGGTTTTTCTGACTTACATTTCGTGA  
TTTTCAGAAAATTTCTTTACGGGTGGAAGCCAATTTACATGGATTAACCCTCTATGACACTG  
CACCTTGCCCTATTAACAATGAACGAACACGGCTACTTTCAGAGATATTTGATGAAAGGAT  
AAAATATTTCTGTAATGATTATGATTCTCAGGGATTGGGGAAAGGTTACAGAAAGTTGCTTA  
TTCTTCTCTGAAATTTTCAACCACTTAATCAAGGCTGACAGTAACACTGATGAATGCTGATA  
ATCAGGAAACATGAAAGAAGCCATTTGATAGATTATTCTAAAGGATATCATCAAGAAGACTA  
TTAAAAACACCTATGCCTATACTTTTTTATCTCAGAAAATAAAGTCAAAAGACTATG

FIGURE 15

NWWFQQGLSFLPSALVIWTSAAFIFSYITAVTLHHIDPALPYISDTGTVAPEKCLFGAMLNI  
AAVLCIATIIYVRYKQVHALSPEENVIIKLNKAGLVLGILSCLGLSIVANFQKTTLFAAHVSG  
AVLTFGMGSLYMFVQTILSYQMOPKIHGKQVFWIRLLLVIWCGVSALSMLTCSSVLHSGNFG  
TDLEQKLHWNPEDKGYVLHMITTAAEWSMSFSFFGFFLTYYIRDFQKISLRVEANLHGLTLYD  
TAPCPINNERTRLLSRDI



FIGURE 16

CGGACGCTTGGGCNGCGCCAGCGGCCAGCGCTAGTCGGTCTGGTAAGTGCCTGATGCCGAGT  
TCCGTCTCTCGGGTCTTTTCCTGGTCCCAGGCAAAGCGGAGCGGAGATCCTCAAACGGCCTA  
GTGCTTCGCGCTTCCGGAGAAAAATCAGCGGTCTAATTAATTCCTCTGGTTTGTTGAAGCAGT  
TACCAAGAATCTTCAACCCTTTCCACAAAAGCTAATTGAGTACACGTTCTGTTGAGTACA  
CGTTCCTGTTGATTTACAAAAGGTGCAGGTATGAGCAGGTCTGAAGACTAACATTTTGTGAA  
GTTGTAAAAACAGAAAACCTGTTAGAAATGTGGTGGTTTCAGCAAGGCCTCAGTTTCCTTCCT  
TCAGCCCTTGTAATTTGGACATCTGCTGCTTTTCATATTTTCATACATTACTGCAGTAACACT  
CCACCATATAGACCCGGCTTTACCTTATATCAGTGACACTGGTACAGTANC

FIGURE 17

CCCACGCGTCCGCCCCGCGCTGCGTCCCGGAGTGCAAGTGAGCTTCTCGGCTGCCCCGCGGG  
CCGGGGTGCGGAGCCGACATGCGCCCCGCTTCTCGGCCTCCTTCTGGTCTTCGCCGGCTGCAC  
CTTCGCCTTGTACTTGCTGTGACGCGACTGCCCCGCGGGCGGAGACTGGGCTCCACCGAGG  
AGGCTGGAGGCAGGTGCTGTGGTTCCCCTCCGACCTGGCAGAGCTGCGGGAGCTCTCTGAG  
GTCCTTCGAGAGTACCGGAAGGAGCACCAGGCCTACGTGTTCTGCTCTTCTGCGGCGCCTA  
CCTCTACAAACAGGGCTTTGCCATCCCCGGCTCCAGCTTCCTGAATGTTTTAGCTGGTGCCT  
TGTTTGGGCCATGGCTGGGGCTTCTGCTGTGCTGTGTGTTGACCTCGGTGGGTGCCACATGC  
TGCTACCTGCTCTCCAGTATTTTTGGCAAAACAGTTGGTGGTGTCTACTTTCTGATAAAGT  
GGCCCTGCTGCAGAGAAAGGTGGAGGAGAAAGAAACAGCTTGTTTTTTTTCTTATTGTTTT  
TGAGACTTTTCCCCATGACACCAAACCTGGTTCTTGAACCTCTCGGCCCCAATTCTGAACATT  
CCCATCGTGCACTTCTTCTCAGTTCTTATCGGTTTGATCCCATATAATTTTCATCTGTGT  
GCAGACAGGGTCCATCCTGTCAACCCTAACCTCTCTGGATGCTCTTTTCTCCTGGGACACTG  
TCTTTAAGCTGTTGGCCATTGCCATGGTGGCATTAAATCCTGGAACCCTCATTAAAAAATTT  
AGTCAGAAACATCTGCAATTGAATGAAACAAGTACTGCTAATCATATACACAGTAGAAAAGA  
CACATGATCTGGATTTTCTGTTTGCCACATCCCTGGACTCAGTTGCTTATTTGTGTAATGGA  
TGTGGTCTCTAAAGCCCCCTCATTGTTTTTGATTGCCTTCTATAGGTGATGTGGACACTGTG  
CATCAATGTGCAGTGTCTTTTCAGAAAGGACACTCTGCTCTTGAAGGTGTATTACATCAGGT  
TTTCAAACCAGCCCTGGTGTAGCAGACACTGCAACAGATGCCTCCTAGAAAATGCTGTTTGT  
GGCCGGGCGCGGTGGCTCACGCCTGTAATCCCAGCACTTTGGGAGGCCGAGGCCGGTGATT  
ACAAGGTCAGGAGTTCAAGACCAGCCTGGCCAAGATGGTGAAATCCTGTCTCTAATAAAAAT  
ACAAAAATTAGCCAGGCGTGGTGGCAGGCACCTGTAATCCCAGCTACTCGGGAGGCTGAGGC  
AGGAGAATTGCTTGAACCAAGGTGGCAGAGGTTGCAGTAAGCCAAGATCACACCACTGCACT  
CCAGCCTGGGTGATAGAGTGAGACACTGTCTTGAC

FIGURE 18

MRPLLGLLLVFAGCTFALYLLSTRLPGRRLGSTEEAGGRSLWFPSDLAELRELSEVLREYR  
KEHQAYVFLLFCGAYLYKQGFAIPGSSFLNVLAGALFGPWLGLLLCCVLTSVGATCCYLLSS  
IFGQLVVSYPDKVALLQRKVEENRNSLFFLLFLRLFPMTPNWFLNLSAPILNIPIVQFF  
FSVLIGLIPYNFICVQTGSILSTLTSLDALFSWDTVFKLLAIAMVALIPGTLIKKFSQKHLQ  
LNETSTANHIHSRKDT

FIGURE 19

CCGAGGCGGGAGGAGCCCGAGGGGGCGCGAGCCCCGCATGAATCATTGTAGTCAATCATTTT  
CCAGTTCTCAGCCGCTCAGTTGTGATCAAGGGACACGTGGTTTCCGAACTGCCAGCTCAGAA  
TAGGAAAATAACTTGGGATTTTATATTGGAAGACATCGATCTTGCTGCCAACGAGATCAGCA  
TTTATGACAACTTTTCAGAGACTGTTGATTGGTGAGACAGACCGGCCATCAGTGTGGCATG  
TCAGAGAAGGCAATTGAAAAATTTATCAGACAGCTGCTGGAAAAGAATGAACCTCAGAGACC  
CCCCCGCAGTATCCTCTCCTTATAGTTGTGTATAAGGTTCTCGCAACCTTGGGATTAATCT  
TGCTCACTGCCTACTTTGTGATTCAACCTTTTCAGCCCATTAGCACCTGAGCCAGTGCTTTCT  
GGAGCTCACACCTGGCGCTCACTCATCCATCACATTAGGCTGATGTCCTTGCCCATTGCCAA  
GAAGTACATGTGAGAAAATAAGGGAGTTCCTCTGCATGGGGGTGATGAAGACAGACCCCTTTC  
CAGACTTTGACCCCTGGTGGACAAACGACTGTGAGCAGAATGAGTCAGAGCCCATTCTTGCC  
AACTGCACTGGCTGTGCCCAGAAACACCTGAAGGTGATGCTCCTGGAAGACGCCCCAAGGAA  
ATTTGAGAGGCTCCATCCACTGGTGATCAAGACGGGAAAGCCCCTGTTGGAGGAAGAGATTC  
AGCATTTTTTGTGCCAGTACCCTGAGGCGACAGAAGGCTTCTCTGAAGGGTTTTTCGCCAAG  
TGGTGGCGCTGCTTTCCTGAGCGGTGGTTCCCATTTCTTATCCATGGAGGAGACCTCTGAA  
CAGATCACAAATGTTACGTGAGCTTTTTCTGTTTTCACTCACCTGCCATTTCCAAAAGATG  
CCTCTTTAAACAAGTGCTCCTTTCTTCACCCAGAACCTGTTGTGGGGAGTAAGATGCATAAG  
ATGCCTGACCTATTTATCATTGGCAGCGGTGAGGCCATGTTGCAGCTCATCCCTCCCTTCCA  
GTGCCGAAGACATTGTGAGTCTGTGGCCATGCCAATAGAGCCAGGGGATATCGGCTATGTGCG  
ACACCACCCACTGGAAGGTCTACGTTATAGCCAGAGGGGTCCAGCCTTTGGTCATCTGCGAT  
GGAACCGCTTTCTCAGAACTGTAGGAAATAGAACTGTGCACAGGAACAGCTTCCAGAGCCGA  
AAACCAGGTTGAAAGGGGAAAAATAAAAACAAAACGATGAACTGCAAAAA

FIGURE 20

MDLAANEISIIYDKLSETVDLVRQTGHQCGMSEKAIEKFIRQLLEKNEPQRPPQYPLLIVVY  
KVLATLGLILLTAYFVIQPFSPPLAPEPVLGAHTWRSLIHHIRLMSLPIAKKYMSENKGVPL  
HGGDEDRPFPDFDPWWTNDCEQNESEPI PANCTGCAQKHLKVMLLEDAPRKFERLHPLVIKT  
GKPLLEEEIQHFLCQYPEATEGFSEGFFAKWWRCFPERWFFPYWRRPLNRSQMLRELFV  
FTHLPFPKASLNKCSFLHPEPVVGSKMHKMPDLFIIGSGEAMLQLIPPFQCRRCQSVAMP  
IEPGDIGYVDTTHWKVYVIARGVQPLVICDGTAFSEL

FIGURE 21

CCACGGTGTCCGTTCTTCGCCCCGGCGGCAGCTGTCCCCGAGGCGGGAGGAGCCCCGAGGGGCG  
CGAGCCCCGCATGAATCATTGTAGTCAATCATTTTCCAGTTCTCAGCCGTTTCAGTTGTGATC  
AAGGGACACGTGGTTTCCGAAC TGCCAGCTCAGAATAGGAAAATAACTTGGGATTTTATATT  
GGAAGACATGGATCTTGCTGCCAACGAGATCAGCATTTATGACAACTTTTCAGAGACTGTTG  
ATTTGGTGAGACAGACCGGCCATCAGTGTGGCATGT CAGAGAAGGCAATTGAAAAATTTATC  
AGACAGCTGCTGGAAAAGAATGAACCTCAGAGACCCCCCGCAGTATCCTCTCCTTATAGT  
TGTGTATAAGGTTCTCGCAACCTTGGGATTAATCTTGCTCACTGCCTACTTTGTGATTCAAC  
CTTTCAGCCCATTAGCACCTGAGCCAGTGCTTTGTGGAGCTCAC

FIGURE 22

CCCACGCGTCCGCCCCACGCGTCCGGCTGAACACCTCTTCTTTGGAGTCAGCCACTGATGAGG  
CAGGGTCCCCAATTGACAGCTGCAGCAGCTGCAGCAGCTGCAGAGCGCTGCTCCTGGCTGGTG  
CCACTGGTGCACGCTGCTAGACCGTGCCTATGAGCCGCTGGGGCTGCAGTGGGGACTGCC  
CTCCCTGCCACCCACCAATGGCAGCCCCACCTTCTTTGAAGACTTCCAGGCTTTTTGTGCCA  
CACCCGAATGGCGCCACTTCATCGACAAACAGGTACAGCCAACCATGTCCCAGTTTCGAAATG  
GACACGTATGCTAAGAGCCACGACCTTATGTAGGTTTCTGGAATGCCTGCTATGACATGCT  
TATGAGCAGTGGGCAGCGCGCCAGTGGGAGCGCGCCAGAGTCGTGGGCTTCCAGGAGC  
TGGTGCTGGAACCTGCGCAGAGGCGGGCGCGCTGGAGGGGCTACGCTACACGGCAGTGCTG  
AAGCAGCAGGCAACGCAGCACTCCATGGCCCTGCTGCACTGGGGGGCGCTGTGGCGCCAGCT  
CGCCAGCCCATGTGGGGCTGGGCGCTGAGGGACACTCCCATCCCCGCTGGAAACTGTCCA  
GCGCCGAGACATATTACGCATGCGTCTGAAGCTGGTGCCCAACCATCACTTCGACCCTCAC  
CTGGAAGCCAGCGCTCTCCGAGACAATCTGGGTGAGGTTCCCCTGACACCCACCGAGGAGGC  
CTCACTGCCTCTGGCAGTGACCAAGAGGCCAAAGTGAGCACCCACCCAGGTTGCTGCAGG  
AGGACCAGCTCGGCGAGGACGAGCTGGCTGAGCTGGAGACCCGATGGAGGCAGCAGAATG  
GATGAGCAGCGTGAGAAGCTGGTGCTGTGCGCCGAGTGCCAGCTGGTGACGGTAGTGGCCGT  
GGTCCCAGGGCTGCTGGAGGTCACCACACAGAATGTATACTTCTACGATGGCAGCACTGAGC  
GCGTGGAACCGAGGAGGGCATCGGCTATGATTTCCGGCGCCCACTGGCCAGCTGCGTGAG  
GTCCACCTGCGGCGTTTCAACCTGCGCCGTTTCAGCACTTGAGCTCTTCTTTATCGATCAGGC  
CAACTACTTCTCAACTTCCCATGCAAGGTGGGCACGACCCAGTCTCATCTCCTAGCCAGA  
CTCCGAGACCCACGCTGGCCCCATCCCCACCCATACCCAGGTACGGAACCCAGGTGTACTCG  
TGGCTCCTGCGCCTACGGCCCCCTCTCAAGGCTACCTAAGCAGCCGCTCCCCCAGGAGAT  
GCTGCGTGCTCAGGCCTTACCCAGAAATGGGTACAGCGTGAGATATCCAACCTTCGAGTACT  
TGATGCAACTCAACACCATTTGCGGGGCGGACCTACAATGACCTGTCTCAGTACCCTGTGTTT  
CCCTGGGTCTTGACGAGTACGTGTCCCCAACCCCTGGACCTCAGCAACCCAGCCGCTTCCG  
GGACCTGTCTAAGCCCATCGGTGTGGTGAACCCCAAGCATGCCAGCTCGTGAGGGAGAAGT  
ATGAAAGCTTTGAGGACCAGCAGGGACCATTGACAAGTTCCACTATGGCACCCACTACTCC  
AATGCAGCAGGCGTGATGCACTACCTCATCCGCGTGGAGCCCTTCACTCCCTGCACGTCCA  
GCTGCAAAGTGGCCGCTTTGACTGCTCCGACCGGCACTTCCACTCGGTGGCGGCAGCCTGGC  
AGGCACGCTGGAGAGCCCTGCCGATGTGAAGGAGCTCATCCCGGAATTCTTCTACTTTCT  
GACTTCTGGAGAACCAGAACGGTTTTGACCTGGGCTGTCTCCAGCTGACCAACGAGAAGGT  
AGGCGATGTGGTGCTACCCCGTGGGCCAGCTCTCCTGAGGACTTCATCCAGCAGCACCCGCC  
AGGCTCTGGAGTCGGAGTATGTGTCTGCACACCTACACGAGTGGATCGACCTCATCTTTGGC  
TACAAGCAGCGGGGGCCAGCCGCGGAGGAGCCCTCAATGTCTTCTATTACTGCACCTATGA  
GGGGCTGTAGACCTGGACCATGTGACAGATGAGCGGGAACGGAAGGCTCTGGAGGGCATT  
TCAGCAACTTTGGGCAGACTCCCTGTGAGCTGTGAAGGAGCCACATCCAACCTCGGCTCTCA  
GCTGAGGAAGCAGCCCATCGCCTTGACGCGCTGGACACTAATCACTAGCATCTTCCAGCA  
CCTGGACGAACTCAAGGCATTTCTTCGAGAGGTGACTGTGAGTGCCAGTGGGCTGCTGGGCA  
CCACAGCTGGTTGCCCTATGACCGCAACATAAGCAACTACTTCAGCTTCAGCAAAAGACCCC  
ACCATGGGCAGCCACAAGACGCAGCGACTGCTGAGTGGCCCGTGGGTGCCAGGCAGTGGTGT  
GAGTGGAACAAGCACTGGCAGTGGCCCCGATGGAAAGCTGCTATTAGCGGTGGCCACTGGG  
ATGGCAGCCTGCGGGTGACTGCACTACCCCGTGGCAAGCTGTTGAGCCAGCTCAGTGCCAC  
CTTGATGTAGTAACCTGCCTTGCACTGGACACCTGTGGCATCTACCTCATCTCAGGCTCCCG  
GGACACCACGTGCATGGTGTGGCGGCTCCTGCATCAGGGTGGTCTGTGAGTAGGCTGGCAC  
CAAAGCCTGTGCAAGTCTGTATGGGCATGGGGCTGCAGTGAGCTGTGTGGCCATCAGCACT  
GAACTTGACATGGCTGTGTCTGGATCTGAGGATGGAAGTGTGATCATACACACTGTACGCCG  
CGGACAGTTTGTAGCGGCACTACGGCTCTGGGTGCCACATTCCCTGGACCTATTTTCCACC  
TGGCATTGGGGTCCGAAGGCCAGATTGTGGTACAGAGCTCAGCGTGGGAACGTCTTGGGGCC  
CAGGTACCTACTCCTTGACCTGTATTTCAGTCAATGGGAAGTTGCGGGCTTCACTGCCCCCT  
GGCAGAGCAGCCTACAGCCCTGACGGTGACAGAGGACTTTGTGTTGCTGGGCACCGCCAGT  
GCGCCCTGCACATCCTCCAACATAACACTGCTCCCGGCCGCGCCTCCCTTGCCCATGAAG  
GTGGCCATCCGCAGCGTGGCCGTGACCAAGGAGCGCAGCCACGTGCTGGTGGGCTGGAGGA  
TGGCAAGCTCATCGTGGTGGTCCGCGGCGAGCCCTCTGAGGTGCGCAGCAGCGTTCGCGC  
GGAAGCTGTGGCGTCTCGCGCGCATCTCCAGGTGTCTCGGGAGAGACGGAATAACAAC  
CCTACTGAGGCGCGCTGAACCTGGCCAGTCCGGCTGCTCGGGCCCCGCCCCCGGCAGGCCTG  
GCCGGGAGGCCCCGCCAGAGTCCGGCGGAACACCCCGGGGTGGGCGAGCCAGGGGGTGA  
GCGGGGCCACCTGCCAGCTCAGGGATTGGCGGGCGATGTTACCCCTCAGGGATTGGCG  
GGCGGAAGTCCCGCCCCCTCGCCGGCTGAGGGGCCGCCCTGAGGGCCAGCACTGGCGTCT

FIGURE 23

MSQFEMDTYAKSHDLMSGFWNACYDMLMSSGQRRQWERAQSRRAFQELVLEPAQRRARLEGL  
RYTAVLKQQATQHSMALLHWGALWRQLASPCGAWALRDTPIPRWKLSSAETYSRMRLKLVPN  
HHFDPHLEASALRDNLGEVPLTPTEEASLPLAVTKEAKVSTPPELLQEDQLGEDELAELTP  
MEAAELDEQREKLVLSAECQLVTVVAVVPGLLEVTTQNVYFYDGSTERVETEEGIGYDFRRP  
LAQLREVHLRRFNLRRSALELFFIDQANYFLNFPCKVGTTPVSSPSQTPRPQPGPIPPHTQV  
RNQVYSWLLRLRPPSQGYLSSRSPQEMLRASGLTQKWVQREISNFEYLMQLNTIAGRITYNDL  
SQYPVFPWVLQDYVSPTLDLSNPAVFRDLSKPIGVVNPKAQLVREKYESFEDPAGTIDKFH  
YGTHYSNAAGVMHYLIRVEPFTSLHVQLQSGRFDCCDRQFHSVAAAWQARLESPADVKEIIP  
EFFYFPDFLENQNGFDLGCLQLTNEKVGDVVLPWASSPEDFIQQHRQALESEYVSAHLHEW  
IDLIFGYKQRGPAEEEEALNVFYCYEGAVDLDHVTDERERKALEGIIISNFGQTPCQLLKEP  
HPTRLSAEEAAHRLARLDTNPSIFQHLDLDELKAFFAEVTVSASGLLGTHSWLPYDRNISNYF  
SFSKDPTMGSHKTQRLLSGPWVPGSGVSGQALAVAPDGKLLFSGGHWDGSLRVTALPRGKLL  
SQLSCHLDVVTCLALDTCGIYLSGSRDTCMVWRLLHQGGLSVGLAPKPVQVLYGHGAAVS  
CVAISTELDMAVSGSEDGTVIIHTVRRGQFVAALRPLGATFPGPIFHLALGSEGQIVVQSSA  
WERPGAQVTYSLHLYSVNGKLRASLPLAEQPTALTVTEDFVLLGTAQCALHILQLNTLLPAA  
PPLPMKVAIRSVAVTKERSHVLVGLEDGKLIVVAGQPSEVRSSQFARKLWRSSRRISQVSS  
GETEYNPTAR



FIGURE 24

CGGACGCGTGGGCGGACGCGTGGGGCTGTGAGAAAGTGCCAATAAATACATCATGCAACCC  
CACGGCCACCTTGTGAACTCCTCGTGCCAGGGCTGATGTGCGTCTTCCAGGGCTACTCAT  
CCAAAGGCCTAATCCAACGTTCTGTCTTCAATCTGCAAATCTATGGGGTCTGGGGCTCTTC  
TGGACCCTTAACTGGGTACTGGCCCTGGGCCAATGCGTCCTCGCTGGAGCCTTTGCCTCCTT  
CTACTGGGCCTTCCACAAGCCCCAGGACATCCCTACCTTCCCCTTAATCTCTGCCTTCATCC  
GCACACTCCGTTACCACACTGGGTCAATTGGCATTGTGGAGCCCTCATCCTGACCCTTGTGCAG  
ATAGCCCGGGTCATCTTGGAGTATATTGACCACAAGCTCAGAGGAGTGAGAACCCCTGTAGC  
CCGCTGCATCATGTGCTGTTTCAAGTGCTGCCTCTGGTGTCTGGAAAAATTTATCAAGTTCC  
TAAACCGCAATGCATACATCATGATCGCCATCTACGGGAAGAATTTCTGTGTCTCAGCCAAA  
AATGCGTTCATGCTACTCATGCGAAACATTGTCAGGGTGGTTCGTCTGGACAAAGTCACAGA  
CCTGCTGCTGTTCTTTGGGAAGCTGCTGGTGGTTCGGAGGCGTGGGGGTCTGTCTCTTCTTTT  
TTTTCTCCGGTCGCATCCCGGGGCTGGGTAAAGACTTTAAGAGCCCCACCTCAACTATTAC  
TGGCTGCCCATCATGACCTCCATCCTGGGGGCTATGTATCGCCAGCGGCTTCTTCAGCGT  
TTTCGGCATGTGTGTGGACACGCTCTTCCTCTGCTTCCTGGAAGACCTGGAGCGGAACAACG  
GCTCCCTGGACCGGCCCTACTACATGTCCAAGAGCCTTCTAAAGATTCTGGGCAAGAAGAAC  
GAGGCGCCCCCGGACAACAAGAAGAGGAAGAAGTGAACAGCTCCGGCCCTGATCCAGGACTGC  
ACCCACCCCCACCGTCCAGCCATCCAACCTCACTTCGCCTTACAGGTCTCCATTTTGTGGT  
AAAAAAGGTTTTAGGCCAGGCGCCGTGGCTCACGCCTGTAATCCAACACTTTGAGAGGCTG  
AGGCGGGCGGATCACCTGAGTCAGGAGTTCGAGACCAGCCTGGCCAACATGGTGAAACCTCC  
GTCTCTATTAAAAATACAAAAATTAGCCGAGAGTGGTGGCATGCACCTGTATCCAGCTAC  
TCGGGAGGCTGAGGCAGGAGAATCGCTTGAACCCGGGAGGCAGAGGTTGCAGTGAGCCGAGA  
TCGCGCCACTGCACTCCAACCTGGGTGACAGACTCTGTCTCCAAAACAAAACAAACAA  
AAAGATTTTATTAAAGATATTTTGTTAACCTC

**FIGURE 25**

RTRGRTRGGCEKVPINTSCNPTAHLVNSSCPGLMCVFQGYSSKGLIQRSVFNLQIYGVLG  
LFWTLNWWLALGQCVLAGAFASFYWAFHKPDIPFPLISAFIRTLRYHTGSLAFGALILTLVQ  
IARVILEYIDHKLRGVQNPVARCIMCCFKCCLWCLEKFIKFLNRNAYIMIAIYGKNFCVSAK  
NAFMLLMRNIVRVVLDKVTDLLFFGKLLVVGGVGVLSFFFFSGRIPGLGKDFKSPHLNYY  
WLPIMTSILGAYVIASGFFSVFGMCVDTLFLCFLEDLERNNGSLDRPYMSKSLKILGKKN  
EAPPDNKKRKK

FIGURE 26

GAGTCTTGACCGCCGCCGGGCTCTTGGTACCTCAGCGCGAGCGCCAGGCGTCCGGCCGCCGT  
GGCTATGTTTCGTGTCCGATTTCCGCAAAGAGTTCTACGAGGTGGTCCAGAGCCAGAGGGTCC  
TTCTCTTCGTGGCCTCGGACGTGGATGCTCTGTGTGCGTGCAAGATCCTTCAGGCCTTGTTTC  
CAGTGTGACCACGTGCAATATACGCTGGTTCCAGTTTCTGGGTGGCAAGAACTTGAAACTGC  
ATTTCTTGAGCATAAAGAACAGTTTCATTATTTTATTCTCATAAACTGTGGAGCTAATGTAG  
ACCTATTGGATATTCTTCAACCTGATGAAGACACTATATTCTTTGTGTGTGACTCCCATAGG  
CCAGTCAATGTTCGTCAATGTATACAACGATACCCAGATCAAATTACTCATTAAACAAGATGA  
TGACCTTGAAGTTCCCGCCTATGAAGACATCTTCAGGGATGAAGAGGAGGATGAAGAGCATT  
CAGGAAATGACAGTGATGGGTGAGAGCCTTCTGAGAAGCGCACACGGTTAGAAGAGGAGATA  
GTGGAGCAAACCATGCGGAGGAGGCAGCGGCGAGAGTGGGAGGCCCGGAGAAGAGACATCCT  
CTTTGACTACGAGCAGTATGAATATCATGGGACATCGTCAGCCATGGTGATGTTTGAGCTGG  
CTTGATGCTGTCCAAGGACCTGAATGACATGCTGTGGTGGGCCATCGTTGGACTAACAGAC  
CAGTGGGTGCAAGACAAGATCACTCAAATGAAATACGTGACTGATGTTGGTGTCTGTCAGCG  
CCACGTTTTCCCGCCACAACCACCGGAACGAGGATGAGGAGAACACACTCTCCGTGGACTGCA  
CACGGATCTCCTTTGAGTATGACCTCCGCCTGGTGCTCTACCAGCACTGGTCCCTCCATGAC  
AGCCTGTGCAACACCAGCTATACCGCAGCCAGGTTCAAGCTGTGGTCTGTGCATGGACAGAA  
GCGGCTCCAGGAGTTCCTTGAGACATGGGTCTTCCCCTGAAGCAGGTGAAGCAGAAGTTCC  
AGGCCATGGACATCTCCTTGAAGGAGAATTTGCGGGAAATGATTGAAGAGTCTGCAAATAAA  
TTTGGGATGAAGGACATGCGCGTGACAGTCTTCAGCATTCATTTTGGGTTCAAGCACAAGTT  
TCTGGCCAGCGACGTGGTCTTTGCCACCATGTCTTTGATGGAGAGCCCCGAGAAGGATGGCT  
CAGGGACAGATCACTTCATCCAGGCTCTGGACAGCCTCTCCAGGAGTAACCTGGACAAGCTG  
TACCATGGCCTGGAACCTGCCAAGAAGCAGCTGCGAGCCACCCAGCAGACCATTGCCAGCTGC  
CTTTGCACCAACCTCGTCATCTCCAGGGGCCTTTCTGTACTGCTCTCTCATGGAGGGCAC  
TCCAGATGTCATGCTGTTCTCTAGGCCGGCATCCCTAAGCCTGCTCAGCAAACACCTGCTCA  
AGTCCTTTGTGTGTTTCGACAAAGAACCGGCGCTGCAAACCTGCTGCCCCCTGGTGATGGCTGCC  
CCCCTGAGCATGGAGCATGGCACAGTGACCGTGGTGGGCATCCCCCAGAGACCGACAGCTC  
GGACAGGAAGAACTTTTTTGGGAGGGCGTTTGAGAAGGCAGCGGAAAGCACCAGCTCCCGGA  
TGCTGCACAACCATTTTGACCTCTCAGTAATTGAGCTGAAAGCTGAGGATCGGAGCAAGTTT  
CTGGACGCACTTATTTCCCTCCTGTCTCTAGGAATTTGATTCTTCCAGAATGACCTTCTTATT  
TATGTAACCTGGCTTTCATTTAGATTGTAAGTTATGGACATGATTTGAGATGTAGAAGCCATT  
TTTTATTAAATAAAATGCTTATTTTAGGAAA

FIGURE 27

MFVSDFRKEFYEVVQSQRVLLFVASDVDALCACKILQALFQCDHVQYTLVPVSGWQELETAF  
LEHKEQFHYFILINCGANVDLLDILQPDEDITFFVCDSHRPVNVNVYNDTQIKLLIKQDDD  
LEVPAIEDIFRDEEEDEEHSGNDS DGSEPEKRTRLEEEIVEQTMRRRQRREWEARRRDILF  
DYEQYEHGTSSAMVMFELAWMLSKDLNDMLWWAIVGLTDQWVQDKITQMKYVTDVGVLRH  
VSRHNRNEDEENTLSVDCTRISFEYDLRLVLYQHWSLHDSLNTSYTAARFKLWSVHGQKR  
LQEF LADMGLPLKQVKQKFQAMD ISLKENLREMI EESANKFGMKDMRVQTF SIHFGFKHKFL  
ASDVVFATMSLMESPEKDGSGTDHFIQALDSLRSNLDKLYHGLELAKKQLRATQQTIASCL  
CTNLVISQGPFLYCSLMEGTPDVMLFSRPASLSLLSKHLLKSFVCSTKNRRCKLLPLVMAAP  
LSMEHGTVTTVVGIPPETDSSDRKNFFGRAFEKAAESTSSRMLHNHFDLSVIELKAEDRSKFL  
DALISLLS

FIGURE 28

GTACCTCAGCGCGAGCGCCAGGGCGTCCGGCCGCGGTGGCTATGNTCGTGTCCGATTTCCGCA  
AAGAGTTCTACGAGGTGGTCCAGAGCCAGAGGGTCCTTCTCTTCGTGGCCTCGGANGTGGAT  
GCTCTGTGTGCGTGCAAGATCCTTCAGGCCTTGTTCCAGTGTGACCANGTGCAATATANGCT  
GGTTCCAGTTTCTGGGTGGCAAGAACTTGAAACTGCATTTCTTGAGCATAAAGAACAGTTTC  
ATTATTTTATTCTCATAAACTGTGGAGCTAATGTAGACCTATTGGATATTCTTCAACCTGAT  
GAAGACACTATATTCTTTGTGTGTGACACCCATAGGCCAGTCAATGTTGTCAATGTATACAA  
CGATACCC

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## FIGURE 29

CAGGAACCCCTCTCTTTGGGTCTGGATTGGGACCCCTTTCCAGTACCATTTTTTCTAGTGAAC  
CACGAAGGGACGATACCAGAAACACCCCTCAACCCAAAGGAAATAGACTACAGCCCCAATTG  
GCTGACTTTGGCTATAGAA1AAAGAAAGGAACGAAAAGAGACAGTTTTTTTTTGGAAAGCTAA  
GTCTTCCCTTTATCGAGTCAAGAAACCCCCCTTCTTGAGCTATTTACAGCTTTTAACAATT  
GAGTAAAGTACGCTCCGGTCACCATGGTGACAGCCGCCCTGGGTCCCGTCTGGGCAGCGCTC  
CTGCTCTTTCTCCTGATGTGTGAGATCCGTATGGTGGAGCTCACCTTTGACAGAGCTGTGGC  
CAGCGGCTGCCAACGGTGCTGTGACTCTGAGGACCCCTGGATCCTGCCCATGTATCCTCAG  
CCTCTTCTCCTCCGGCCGCCCCACGCCCTGCCTGAGATCAGACCTACATTAATATCACCATC  
CTGAAGGGTGACAAAGGGGACCCAGGCCCAATGGGCCTGCCAGGGTACATGGGCAGGGAGGG  
TCCCAAGGGGAGCCTTGGCCCTCAGGGCAGCAAGGGTGACAAGGGGAGATGGGCAGCCCCG  
GCGCCCCGTGCCAGAAGCGCTTCTTCGCCCTTCTCAGTGGGCCGCAAGACGGCCCTGCACAGC  
GGCGAGGACTTCCAGACGCTGCTCTTCGAAAGGGTCTTTGTGAACCTTGATGGGTGCTTTGA  
CATGGCGACCGGCCAGTTTGCTGCTCCCCCTGCGTGGCATCTACTTCTTCAGCCTCAATGTGC  
ACAGCTGGAAATTACAAGGAGACGTACGTGCACATTATGCATAACCAGAAAGAGGCTGTATC  
CTGTACGCGCAGCCAGCGAGCGCAGCATCATGCAGAGCCAGAGTGTGATGCTGGACCTGGC  
CTACGGGGACCGCTCTGGGTGCGGCTCTTCAAGCGCCAGCGCAGAAACGCCATCTACAGCA  
ACGACTTCGACACCTACATCACCTTCAGCGGCCACCTCATCAAGGCCGAGGACGACTGAGGG  
CCTCTGGGCCACCCCTCCCGGCTGGAGAGCTCAGGTGCTGGTCCCGTCCCTTGACGGGCTCAG  
TTTGCACTGCTGTGAAGCAGGAAGGCCAGGGAGGTCCCGGGGACCTGGCATCTTGGGGAGA  
CCCTGCTTCTATCTTGGCTGCCATCATCCCTCCAGCCTATTTCTGCTCCTCTCTCTCTCT  
TGGACCTATTTTAAGAAGCTTGCTAACCTAAATATTCTAGAACTTTCCAGCCTCGTAGCCC  
AGCACTTCTCAAACCTTGGAATGCATGCCAATCACCCGGGGTTCGTGTTAAATGCAGATTCT  
GACTCAGCAGGTCTGAGTGGGTCCAGGATTCTGTGTTTCTCATATGTTCTGGGTGATGCTG  
ATGGGGTCAGTCTATGAACCACTGGAGCAACCAGGTTCTAGGACTTTCTCAATATTCTAG  
TACTTTCTGAACATTCTGGAATCCTCCCCACATTCTAGAATTCTCCCAACATTTTTTTTTCT  
TGAGACAGAGTCTTGCTCTGTTGCCCAGGCTAGAGTGCAGTGGTGCAATCTCAGTTCACCTGC  
AACCTCTGCCTCCCGGGTTCAGCGGATTCTTCTGCCTCAGCCTCCCTAGTGGCTGGGATTAC  
AGGCGCCTGCTACCATGCCTGGCTAATTTTTGTATTTTTAGTAGAGATGGGGTTTCACCATA  
TTGGCCAGGCTGGTCTTGAACCTCCTGACTTCAGGTGACCCACCCGCTCTCGGCTCTCAAAAT  
TGCTGGGATTACAGGTGTGAGCCACCGTGCTGGCCAATTCCAACATTCTTAAATTCTCTCAT  
CCCTCCAGGGCTCCCGTGCTATGTTCTCTTTACCCCTTCCCCCTCTTCTCTTGCTCAGGCC  
TGCACCACTGCAGCCACCGTTCATTATTCATTCAATTAACACTGAGCACTCACTCTGTGCT  
GGGTCCCGGGAAGGGTGAGGGGGTCAGACACAGGCCCTGCCCTGCCCTCAGTGAAGTGGCCA  
GTCCAGCCAGGCGGGGAGAGATGTGTACATAGGTTTAAAGCAGACCCAGAGCTCATGGGG  
GCCTGTGTTCTGGGTGTTCAGGTGCTGCTGGTCTCCATTACCCACTGCTCCCAAGGCTGG  
TGGGACGGGTCCCGGTGGCAGGGGCAGGTATCTCCTTCCCGTTCCTCATCCACCTGCCAG  
TGCTCATCGTTACAGCAAACCCAGGGGGCCTTGGCCAGGTCAAGGGTCTGTGAGGAGAGG  
ACCCAGGAGTGTGGGGCATTTGGGGGGTGAAGTGGCCCCCGAAGAATGGAACCCACACCCA  
TAGCTCTCCCCACAGCTGATACGGCATCTGCGAGAAGACCTGCCCTCCTCACTGGGATCCC  
CTTCTGCTCCTCCCAGGGCTCTGCCAGGGCCTTGCTCAGTCCCTTCCACCAAAGTCATCT  
GAACTTCCGTTTCCCCAGGGCCTCCAGCTGCCCTCAGACACTGATGTCTGTCCCCAGGTGCT  
CTCTGCCCCCTCATGCCCCCTCTCACCGGCCAGTGCCCCGACTCTCCAGGCTTTATCAAGGTG  
CTAAGGCCCGGGTGGGCAGCTCCTCGTCTCAGAGCCCTCCTCCGGCCTGGTGCTGCCTTTAC  
AAACACCTGCAGGAGAAGGGCCACGGAAGCCCCAGGCTTTAGAGCCCTCAGCAGGTCTGGGG  
AGCTAGAGCAAAGGAGGGACCTCAGGCCTTCCGTTTCTTCTTCCAGGGTGGGGTGGCCTGGT  
GTTCCCCCTAGCCTTCCAAACCCAGGTGGCCTGCCCTTCTCCCCAGAGGGAGGCGCCTCCGC  
CCATTGGTGCTCATGCAGACTCTGGGGCTGAGGTGCCCGGGGGTGATCTCTGGTGCTCAC  
AGCCGAGGGAGCCGTGGCTCCATGGCCAGATGACGGAACAGGGTCTGACCAAGTGCCAGGA  
AGACCTGTGCTATAAACACCCCTGCCTGATCCTGCCCTGCCTGACCCCGCCACGCCCTGCC  
GTCCAGCATGATTAAAGAATGCTGTCTCCTCTTGAAAAAAAAAAAAAAAAA

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FIGURE 30

MVTAALGPVWAALLLFLLMCEIRMVELTFDRAVASGCQRCCDSEDPLDPAHVSSASSSGRPH  
ALPEIRPYINITILKGDKGDPGPMGLPGYMGREGPQGEPPGQSGDKGEMGSPGAPCQKRF  
FAFSVGRKTALHSGEDFQTLLFERVFVNLDGCFDMATGQFAAPLRGIYFFSLNVHSWNYKET  
YVHIMHNQKEAVILYAQPSESRIMQSQSVMLDLAYGDRVWVRLFKRQRENAIYSNDFDTYIT  
FSGHLIKAEDD

**Important features:**

**Signal peptide:**

amino acids 1-20

**N-glycosylation site.**

amino acids 72-75

**Clq domain proteins.**

amino acids 144-178, 78-111 and 84-117

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FIGURE 31

ACTCGAACGCAGTTGCTTCGGGACCCAGGACCCCCTCGGGCCCGACCCGCCAGGAAAGACTG  
AGGCCGCGGCCTGCCCCGCCCCGGCTCCCTGCGCCGCGCGCCTCCCGGGACAGAAGATGTG  
CTCCAGGGTCCCTCTGCTGCTGCCGCTGCTCCTGCTACTGGCCCTGGGGCCTGGGGTGCAGG  
GCTGCCCATCCGGCTGCCAGTGCAGCCAGCCACAGACAGTCTTCTGCACTGCCCGCCAGGGG  
ACCACGGTGCCCCGAGACGTGCCACCCGACAGGTGGGGCTGTACGTCTTTGAGAACGGCAT  
CACCATGCTCGACGCAGGCAGCTTTGCCGGCCTGCCGGGCCTGCAGTCTCTGGACCTGTAC  
AGAACCAGATCGCCAGCCTGCCAGCGGGGTCTTCCAGCCACTCGCCAACCTCAGCAACCTG  
GACCTGACGGCCAACAGGCTGCATGAAATCACCAATGAGACCTTCCGTGGCCTGCGGCGCCT  
CGAGCGCCTCTACCTGGGCAAGAACCGCATCCGCCACATCCAGCCTGGTGCCTTCGACACGC  
TCGACCGCCTCCTGGAGCTCAAGCTGCAGGACAACGAGCTGCGGGCACTGCCCCGCTGCGC  
CTGCCCCGCTGCTGCTGCTGGACCTCAGCCACAACAGCCTCCTGGCCCTGGAGCCCGGCAT  
CCTGGACACTGCCAACGTGGAGGCGCTGCGGCTGGCTGGTCTGGGGCTGCAGCAGCTGGACG  
AGGGGCTCTTCAGCCGCTTGCGCAACCTCCAGACCTGGATGTGTCCGACAACAGCTGGAG  
CGAGTGCCACCTGTGATCCGAGGCCTCCGGGGCCTGACGCGCCTGCGGCTGGCCGGCAACAC  
CCGCATTGCCCAGCTGCGGCCCGAGGACCTGGCCGGCCTGGCTGCCCTGCAGGAGCTGGATG  
TGAGCAACCTAAGCCTGCAGGCCCTGCCTGGCGACCTCTCGGGCCTCTTCCCCCGCCTGCGG  
CTGCTGGCAGCTGCCCCGAACCCCTTCAACTGCGTGTGCCCCCTGAGCTGGTTTGGCCCCCTG  
GGTGCGGAGAGCCACGTCACTAGGCCAGCCCTGAGGAGACGCGCTGCCACTTCCCCCCCA  
AGAACGCTGGCCGGCTGCTCCTGGAGCTTGACTACGCCGACTTTGGCTGCCACCCACC  
ACCACAGCCACAGTGCCCAACCACGAGGCCGTGGTGCGGGAGCCACAGCCTTGTCTTCTAG  
CTTGGCTCCTACCTGGCTTAGCCCCACAGCGCCGCACTGAGGCCCCAGCCCCGCTCCA  
CTGCCCCACCGACTGTAGGGCCTGTCCCCAGCCCCAGGACTGCCACCGTCCACCTGCCTC  
AATGGGGGCACATGCCACCTGGGGACACGGCACCACTGGCGTGCTTGTGCCCCGAAGGCTT  
CACGGGCCTGTACTGTGAGAGCCAGATGGGGACAGGGGACACGGCCAGCCCTACACCAGTCA  
CGCCGAGGCCACCACGGTCCCTGACCCTGGGCATCGAGCCGGTGAGCCCCACCTCCCTGCGC  
GTGGGGCTGCAGCGCTACCTCCAGGGGAGCTCCGTGACGCTCAGGAGCCTCCGTCTCACCTA  
TCGCAACCTATCGGGCCCTGATAAGCGGCTGGTGACGCTGCGACTGCCTGCCTCGCTCGCTG  
AGTACACGGTCACCCAGCTGCGGCCCAACGCCACTTACTCCGTCTGTGTATGCCTTTGGGG  
CCCCGGGCGGTGCCGAGGGCGAGGAGGCTGCGGGGAGGGCCATACACCCCGAGCCGTCCA  
CTCCAACCCAGCCCCAGTCACCCAGGCCCGCGAGGGCAACCTGCCGCTCCTCATTGCGCCG  
CCCTGGCCGCGGTGCTCCTGGCCGCGCTGGCTGCGGTGGGGGCAGCCTACTGTGTGCGGCGG  
GGGCGGGCCATGGCAGCAGCGGCTCAGGACAAAGGGCAGGTGGGGCCAGGGGCTGGGCCCT  
GGAACCTGGAGGGAGTGAAGGTCCCCTTGGAGCCAGGCCCGAAGGCAACAGAGGGCGGTGGAG  
AGGCCCTGCCACGCGGTCTGAGTGTGAGGTGCCACTCATGGGCTTCCAGGGCCTGGCCTC  
CAGTCACCCCTCCACGCAAGCCCTACATCTAAGCCAGAGAGAGACAGGGCAGCTGGGGCCG  
GGCTCTCAGCCAGTGAGATGGCCAGCCCCCTCCTGCTGCCACACCAGTAAGTTCTCAGTCC  
CAACCTCGGGGATGTGTGCAGACAGGGCTGTGTGACCACAGCTGGGCCCTGTTCCCTCTGGA  
CCTCGGTCTCCTCATCTGTGAGATGCTGTGGCCCCAGCTGACGAGCCCTAACGTCCCCAGAAC  
CGAGTGCCATGAGGACAGTGTCCGCCCTGCCCTCCGCAACGTGCAGTCCCTGGGCACGGCG  
GGCCCTGCCATGTGCTGGTAACGCATGCCTGGGTCCCTGCTGGGCTCTCCCACTCCAGGCGGA  
CCCTGGGGGCCAGTGAAGGAAGCTCCCGGAAAGAGCAGAGGGAGAGCGGGTAGGCGGCTGTG  
TGACTCTAGTCTTGGCCCCAGGAAGCGAAGGAACAAAAGAAAAGTGGAAAGGAAGATGCTTTA  
GGAACATGTTTTGCTTTTTTAAAATATATATATTTATAAGAGATCCTTTCCCATTTATTCTG  
GGAAGATGTTTTCAAACCTCAGAGACAAGGACTTTGGTTTTTGTAAAGACAAACGATGATATG  
AAGGCCTTTTGTAAAGAAAAAATAAAGATGAAGTGTGAAA



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FIGURE 32

MCSRVP LLLP LLLLLALGPGVQGCPSGCQCSQPQT V FCTARQGT TVPRDVPPDTVGLYVFEN  
GITMLDAGSFAGLPGLQLLDLSQNQIASLPSGVFQPLANLSNLDLTANRLHEITNETFRGLR  
RLERLYLGKNRIRHIQPGAFDTLDRLLELKLQDNELRALPPLRLPRLLLLDLSHNSLLALEP  
GILDTANVEALRLAGLGLOQLDEGLFSRLRNLDLDVSDNQLERVPPVIRGLRGLTRLRLAG  
NTRIAQLRPEDLAGLAALQELDVSNSLQALPGDLSGLFPRLRLAAARNPFNCVCPLSWFG  
PWVRESHVTIASPEETRCHFPKNAGRLLLELDYADFGCPATTTTATVPTTRPVVREPTALS  
SSLAPTWLSPTAPATEAPSPSTAPPTVGPVPQPDCCPSTCLNGGTCHLGTRHHLACLCPE  
GFTGLYCESQMGQGT RPSPTPVTPRP RSLTLGIEPVSPSTSLRVGLQRYLQGSSVQLRSLRL  
TYRNLSGPDKRLVTLRLPASLAEYTVTQLRPNATYSVCMPLGPGRVPEGEEACGEAHTPPA  
VHSNHAPVTQAREGNLPLLIAPALAAVLLAALAAVGAAYCVRRGRAMAAAAQDKGQVGPAG  
PLELEGVKVPLEPGPKATEGGGEALPSGSECEVPLMGFPGLQSPLHAKPYI

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FIGURE 33

GAATCATCCACGCACCTGCAGCTCTGCTGAGAGAGTGAAGCCGTGGGGGTTTTGAGCTCAT  
CTTCATCATTATGAGGAAATAAGTGGTAAATCCTTGGAAATACAATGAGACTCAACAG  
AAACATTTACATATTTGTAGTATTGTTATGACAGCAGAGGGTGATGCTCCAGAGCTGCCAG  
AAGAAAGGGAACGTGATGACCAACTGCTCCAACATGTCTTAAGAAAGGTTCCCGCAGACTTG  
ACCCAGCCACAACGACACTGGATTTATCCTATAACCTCCTTTTTCAACTCCAGAGTTCAGA  
TTTTCTATTCTGTCTCCAACTGAGAGTTTTGATTCTATGCCATAACAGAATTCAACAGCTGG  
ATCTCAAAACCTTTGAATTCACAAGGAGTTAAGATATTTAGATTTGTCTAATAACAGACTG  
AAGAGTGTAACCTGGTATTTACTGGCAGGTCTCAGGTATTTAGATCTTTCTTTAATGACTT  
TGACACCATGCTTATCTGTGAGGAAGCTGGCAACATGTCACACCTGGAAATCCTAGGTTTGA  
GTGGGGCAAAAATACAAAATCAGATTTCCAGAAAATTGCTCATCTGCATCTAAATACTGTC  
TTCTTAGGATTGAGAACTCTTCTCATTATGAAGAAGGTAGCCTGCCCATCTTAAACACAAC  
AAAATGTCACATTGTTTACCAATGGACACAAATTTCTGGGTTCTTTTGCGTGATGGAATCA  
AGACTTCAAAAATATTAGAAATGACAAATATAGATGGCAAAAGCCAATTTGTAAGTTATGAA  
ATGCAACGAAATCTTAGTTTAGAAAATGCTAAGACATCGGTTCTATTGCTTAATAAAGTTGA  
TTTACTCTGGGACGACCTTTTCTTATCTTACAATTTGTTTGGCATAACATCAGTGGAACACT  
TTCAGATCCGAAATGTGACTTTTGGTGGTAAGGCTTATCTTGACCACAATTCAATTTGACTAC  
TCAAATACTGTAATGAGAACTATAAAATTTGGAGCATGTACATTTAGAGTGTTTTACATTCA  
ACAGGATAAAATCTATTTGCTTTTGACCAAAATGGACATAGAAAACCTGACAATATCAAATG  
CACAAATGCCACACATGCTTTTCCCGAATTATCTACGAAATTCGAATTTAAATTTTGCC  
AATAATATCTTAACAGACGAGTTGTTTAAAAGAACTATCCAACCTGCCTCACTTGAAAACCTCT  
CATTTTGAATGGCAATAAACTGGAGACACTTTCTTTAGTAAGTTGCTTTGCTAACAACACAC  
CCTTGGAACTTGGATCTGAGTCAAAATCTATTACAACATAAAAATGATGAAAATTTGCTCA  
TGGCCAGAACTGTGGTCAATATGAATCTGTCTACATAAATAAATTGTCTGATTCTGTCTTCAG  
GTGCTTGCCCAAAAGTATTCAAATACTTGACCTAAAATAAACCAGAAATCCAACTGTACCTA  
AAGAGACTATTCTGATGGCCTTACGAGAACTAAATATTGCATTTAATTTCTAACTGAT  
CTCCCTGGATGCAGTCATTTAGTAGACTTTAGTTCTGAACATTGAAATGAACTTCATTCT  
CAGCCCATCTCTGGATTTTGTTCAGAGCTGCCAGGAAGTTAAACTCTAAATGCGGGAAGAA  
ATCCATTCCGGTGTACCTGTGAATTAATAAATTTTCAATTCAGCTTGAAACATATTTCAGAGGT  
ATGATGGTTGGATGGTCAGATTCATACACCTGTGAATACCCTTTAAACCTAAGGGGAAGTAG  
GTTAAAAGACGTTCTCTCCACGAATTATCTTGCAACACAGCTCTGTTGATTGTCAACATTG  
TGTTTATTATGCTAGTTCTGGGGTTGGCTGTGGCCTTCTGCTGTCTCCACTTTGATCTGCCC  
TGGTATCTCAGGATGCTAGGTCAATGCACACAAACATGGCACAGGTTAGGAAAACAACCCA  
AGAACAACCTCAAGAGAAATGTCCGATTCCACGCATTTATTTATACAGTGAAACATGATTCTC  
TGTGGGTGAAGAATGAATTGATCCCCAATCTAGAGAAGGAAGATGGTTCTATCTTGATTGTC  
CTTTATGAAAGCTACTTTGACCCTGGCAAAAGCATTAGTGAAAATATTGTAAGCTTCATTGA  
GAAAAGCTATAAGTCCATCTTTGTTTTGTCTCCCACTTTGTCCAGAATGAGTGGTGCCATT  
ATGAATTTACTTTGCCCACCACAATCTCTCCATGAAAATTTCTGATCATATAATCTTATC  
TTACTGGAAACCCATTCCATTCTATTGCATTCCACCAGGTATCATAAACTGAAAGCTCTCCT  
GGAAAAAAGCATACTTGGAAATGGCCCAAGGATAGGCGTAAATGTGGGCTTTTCTGGGCAA  
ACCTTCGAGCTGCTATTAATGTTAATGTATTAGCCACCAGAGAAATGTATGAACTGCAGACA  
TTCACAGAGTTAAATGAAGAGTCTCGAGGTTCTACAATCTCTCTGATGAGAACAGATTGTCT  
ATAAATCCCAAGTCTTTGGGAAGTTGGGGACCACATACACTGTTGGGATGTACATTGATA  
CAACCTTTATGATGGCAATTTGACAATATTTATTAATAAATAAATAAATGGTTATTCCCTTCATA  
TCAGTTTCTAGAAGGATTTCTAAGAAATGTATCTTATAGAAACACCTTCACAAGTTTATAAGG  
GCTTATGGAAGGAGGTTTATCTCCAGGATTGTTTATAATCATGAAAATGTGGCCAGGTGC  
AGTGGCTCACTCTTGTAAATCCAGCACTATGGGAGGCCAAGGTGGGTGACCCACGAGGTCAA  
GAGATGGAGACCATCTTGCCCAACATGGTGAAACCTGTCTCTACTAAAAATACAAAAATTA  
GCTGGGCGTGATGGTGCACGCCTGTAGTCCAGCTACTTGGGAGGCTGAGGCAGGAGAATCG  
CTTGAACCCGGGAGGTGGCAGTTGCAGTGAGCTGAGATCGAGCCACTGCACTCCAGCCTGGT  
GACAGAGCGAGACTCCATCTCAAAAAAAGAAAAAAGAAAAAATGGAAAAACATCC  
TCATGGCCACAAAAAAGGTCTAATTCAATAAATTATAGTACATTAAATGTAATATAATATTA  
CATGGCACTAAAAAAGAAATAAGGTAGCTGTATATTTCTGGTATGGAAAAAATATAATAT  
GTTATAAACTATTAGGTTGGTGCAAACTAATTGTGGTTTTTGGCATTGAAATGGCATTGAA  
ATAAAGTGTAAAGAAATCTATACCAGATGTAGTAACAGTGGTTTGGGTCTGGGAGGTTGGA  
TTACAGGGAGCATTGATTTCTATGTTGTGATTCTATAATGTTTGAATGTTTAGAATGA  
ATCTGTATTTCTTTTATAAGTAGAAAAAATAAAGATAGTTTTTACAGCCT

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FIGURE 34

MRLIRNIYIFCSI VMTAEGDAPELPEERELMTNCSNMSLRKVPADLTPATTTLDLSYNLLFQ  
LOSSDFHSVSKLRVLILCHNRIQQDLKTFEFNKELRYLDLSNNRLKSVTWYLLAGLRYLDL  
SFNDFDTMPICEEAGNMSHLEILGLSGAKIQKSDFQKIAHLHLNTVFLGFRTLPHYEEGSLP  
ILNTTKLHIVLPMDTNFWVLLRDGIKTSKILEMTNIDGKSQFVSYEMQRNLSLENAKTSVLL  
LNKVDLLWDDLFLILQFVWHTSVEHFQIRNVTFGGKAYLDHNSFDYSNTVMRTIKLEHVHFR  
VFYIQQDKIYLLLT KMDIENLTISNAQMPHMLFPNYPTKFQYLN FANNILTDELFPKRTIQLP  
HLKTLILNGNKLETLSLVSCFANNTPLEHLDLSQNLLQHKN DENC SWPETVVNMNLSYNKLS  
DSVFRCLPKSIQILD LNNNIQTVPKETIHLMALRELNIAFNFLTDLPGCSHFSRLSVLNIE  
MNFILSPSLDFVQSCQEVKTLNAGRNPFRCTCELKNFIQLETYSEVMMVGWSDSYTCEYPLN  
LRGTRLKDVHLHELSCNTALLIVTIVVIMLVGLAVAF CCLHFDLPWYLRMLGQCTQTWHRV  
RKTTQEQLKRNVRFHAFISYSEHDSLWVKNELIPNLEKEDGSILICLYESYFDPGKSISENI  
VSFIEKSYKSIFVLSPNFVQNEWCHYEFYFAHNL FHENS DHII LILLEPIPFYCIPTRYHK  
LKALLEKKAYLEWPKDRRKCGLFWANLRAA INNVNVLATREMYELQTFTELNEESRGSTISLM  
RTDCL

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FIGURE 35A

GGGGGCTTTCTTGGGCTTGGCTGCTTGGAACACCTGCCTCCAAGGACCGGCCTCGGAGGGGT  
CGCCGGGAAAGGGAGGGAAGAAGGAAGGGCGGGGCCGGCCCCCTGCGCCCCCGCCGCGCCT  
CTGCGCGCCCCCTGTCCGCCCCGGCCCCAGCCAGCCAGCCCGCGGGCCGGTCAACACGCGCA  
GCCAGCCGGCCGCTCCCGCGCCCCAAGCGCGCCGCTCTGCTGTGCCCTGCGCCCTTGCCCCG  
CGCCAGCTTCTGCGCCCGAGCCCGCCCCGGCGCCCCCGGTGACCGTGACCTGCCCTGGGCG  
CGGGGCGGAGCAGGCATGTCCCCCGCGGGGACCGCTACCCAGCGCTGGCCCTGGTGCTCCT  
GGCAGTGACCTGGCCGGGTGCGAGCCAGGGCGCAGCCCTCGAGGACCTGATTATTACG  
GGCAGGAGATCTGGAGCCGGGAGCCCTACTACGCGCGCCCGAGCCCGAGCTCGAGACCTTC  
TCTCCGCGCTGCTGCGGGGCCGGGGAGGAGTGGGAGCGGCGCCCGAGGAGCCAGGCC  
GCCCAAGAGGGCCACCAAGCCCCAAGAAAGCTCCCAAGAGGGAGAAGTCGGCTCCGGAGCCGC  
CTCCACCAGGTAAACACAGCAACAAAAAGTTATGAGAACCAAGAGCTCTGAGAAGGCTGCC  
AACGATGATCACAGTGTCGTGTGGCCCGTGAAGATGTGAGAGAGAGTTGCCACCTCTTGG  
TCTGGAAACCTTAAAAATCACAGACTTCCAGCTCCATGCCTCCACGGTGAAGCGCTATGGCC  
TGGGGGCACATCGAGGGGAGACTCAACATCCAGGCGGGCATTAAATGAAAATGATTTTTATGAC  
GGAGCGTGGTGCGCGGGAAGAAATGACCTCCAGCAGTGGATTGAAGTGGATGCTCGGCGCCT  
GACCAGATTCACTGGTGTCTCACTCAAGGGAGGAACTCCCTCTGGCTGAGTGACTGGGTGA  
CATCCTATAAGGTCATGGTGAGCAATGACAGCCACACGTGGGTCACTGTAAAGAATGGATCT  
GGAGACATGATATTTGAGGGAAACAGTGAGAAGGAGATCCCTGTTCTCAATGAGCTACCCGT  
CCCCATGGTGGCCCGCTACATCCGCATAAACCCCTCAGTCCTGGTTTTGATAATGGGAGCATCT  
GCATGAGAATGGAGATCCTGGGCTGCCACTGCCAGATCCTAATAATTATTATCACCGCCGG  
AACGAGATGACCACCACTGATGACCTGGATTTTAAGCACCACAATTATAAGGAAATGCGCCA  
GTTGATGAAAGTTGTGAATGAAATGTGTCCCAATATCACCAGAATTTACAACATTGAAAAA  
GCCACCAGGGCCTGAAGCTGTATGCTGTGGAGATCTCAGATCACCCCTGGGGAGCATGAAGTC  
GGTGAGCCCGAGTTCCACTACATCGCGGGGGCCACGGCAATGAGGTGCTGGGCCGGGAGCT  
GCTGCTGCTGCTGGTGAGTTCGTGTGTGAGGAGTACTTGGCCCGGAATGCGCGCATCGTCC  
ACCTGGTGGAGGAGACGCGGATTACGTCCTCCCTCCCTCAACCCCGATGGCTACGAGAAG  
GCCTACGAAGGGGGCTCGGAGCTGGGAGGCTGGTCCCTGGGACGCTGGACCCACGATGGAAT  
TGACATCAACAACAATTTCTGATTTAAACACGCTGCTCTGGGAGGCAGAGGATCGACAGA  
ATGTCCCCAGGAAAGTTCCCAATCACTATATTGCAATCCCTGAGTGGTTTTCTGTGCGAAAT  
GCCACGGTGGCTGCCGAGACCAGAGCAGTCATAGCCTGGATGGAAAAAATCCCTTTTGTGCT  
GGGCGGCAACCTGCAGGGCGGCGAGCTGGTGGTGGCGTATCCCTACGACCTGGTGCGGTCCC  
CCTGGAAGACGCAGGAACACACCCCCACCCCGATGACCACGTGTTCCGCTGGCTGGCCTAC  
TCCTATGCCTCCACACACCGCCTCATGACAGACGCCCGGAGGAGGGTGTGCCACACGGAGGA  
CTTCCAGAAGGAGGAGGGCACTGTCAATGGGGCCTCCTGGCACACCGTCGCTGGAAGTCTGA  
ACGATTTAGCTACCTTCATACAACTGCTTCGAACTGTCCATCTACGTGGGCTGTGATAAA  
TACCCACATGAGAGCCAGCTGCCCGAGGAGTGGGAGAATAACCGGGAATCTCTGATCGTGTT  
CATGGAGCAGGTTTCATCGTGGCATTAAAGGCTTGGTGAGAGATTACATGGAAAAGGAATCC  
CAAACGCCATTATCTCCGTAGAAGGCATTAACCATGACATCCGAACAGCCAACGATGGGGAT  
TACTGGCGCCTCCTGAACCTGGAGAGTATGTGGTCACAGCAAAGGCCGAAGGTTTCACTGC  
ATCCACCAAGAACTGTATGGTTGGCTATGACATGGGGGCCACAAGGTGTGACTTCACACTTA  
GCAAAACCAACATGGCCAGGATCCGAGAGATCATGGAGAAGTTTGGGAAGCAGCCCGTCAGC  
CTGCCAGCCAGGCGCTGAAGCTGCGGGGGCGGAAGAGACGACAGCGTGGGTGAACCTCCTG  
GGCCCTTGAGACTCGTCTGGGACCCATGCAATTAACCAACCTGGTAGTAGCTCCATAGTG  
GACTCACTCACTGTTGTTTCTCTGTAATTCAAGAAGTGCCTGGAAGAGAGGGTGCATTGTG  
AGGCAGGTCCCAAAGGGAAGGCTGGAGGCTGAGGCTGTTTTCTTTTCTTTGTTCCATTTA  
TCCAAATAACTTGACAGAGCAGCAGAGAAAAGCTGATGGGAGTGAGAGAACTCAGCAAGCC  
AACCTGGGAATCAGAGAGAGAAGGAGAAGGAGGGGAGCCTGTCCGTTACAGAGCCTCTGGCTGC

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FIGURE 35B

ATAGAAAAGGATTCTGGTGCTTCCCCTGTTTGCCTGGCAGCAAGGGTTCCACGTGCATTTGC  
AATTTGCACAGCTAAAATTGCAGCATTTCCCCAGCTGGGCTGTCCCAAATGTTACCATTTGA  
GATGCTCCCAGGCGTCCTAAGAGAATCCACCCTCTCTGGCCCTGGGACATTGCAAGCTGCTA  
CAAATAAATTCTGTGTTCTTTTGACAATAGCGTCATTGCCAAGTGCACATCAGTGAGCCTCT  
TGAATCTGTTTAGTCTCCTTTTTCAACAAAGGAGTGTTGTTTGCAGAAAAGGAGAGAGAGGCTGA  
GATCATTCAGGAGTTTGTGTTGGGAGCAAGCATGGAGCTTCTTGACAAAATTCTGGGTCCATA  
AACAAACCCCAAGTCCCTGCTGATCCAGTAGCCCTGGAGGTTCCCCAGGTAGGGAGAGCCA  
GAGGTGCCAGCCTTCTGAAGGGCCAGAAAATTTAGCCTGGATCTCCTCTTTTACCTGCTAG  
GACTGGAAAGAGCCAGAAGTGGGGTGGCCTGAAGCCCTCTCTCTGCTTGAGGTATTGCCCCCT  
GTGTGGAATTGAGTGCTCATGGGTGGCCTCATATCAGCCTGGGAGTTATTTTTGATATGTA  
GAATGCCAGATCTTCCAGATTAGGCTAAATGTAATGAAAACCTCTTAGGATTATCTGTGGAG  
CATCAGTTTGGGAAGAATTATTGAATTATCTTGCAAGAAAAAAGTATGTCTCACTTTTTTGT  
AATGTTGCTGCCTCATTGACCTGGGAAAAATGAAAAAAAAAATAAGCAAATGGTAAGACC  
CTTAAA

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FIGURE 36

MSRPGTATPALALVLLAVTLAGVGAQGALEDPDYYGQEIWSREPYARPEPELETFSPPLP  
AGPGEEWERRPQEPRPPKRATKPKKAPKREKSAPEPPPPGKHSNKKVMRTKSSEKAANDDHS  
VRVAREDVRESCPPLGLETLKITDFQLHASTVKRYGLGAHRGRLNIQAGINENDFYDGAWCA  
GRNDLQQWIEVDARRLTRFTGVITQGRNSLWLSDWVTSYKVMVSNDSTWVTVKNGSGDMIF  
EGNSEKEIPVLNELPVPMPVARYIRINPQSWFDNGSICMRMEILGCPLPDPNNYYHRRNEMTT  
TDDLDFKHHNYKEMRQLMKVVNEMCPNITRIYNIGKSHQGLKLYAVEISDHPGEHEVGEPEF  
HYIAGAHGNEVLGRELLLLLVQFVCQEYLARNARIVHLVEETRIHVLP SLNPDGYEKAYEGG  
SELGGWSLGRWTHDGIDINNNFPDLNTLLWEAEDRQNVPRKVPNHYIAIPEWFLSENATVAA  
ETRAVIAWMEKIPFVLGGNLQGGEVLVAYPYDLVRSPWKTQEHTPTPDDHVFRWLAYSAST  
HRLMTDARRRVCHTEDFQKEEGTVNGASWHTVAGSLNDFSYLHTNCFELSIYVGCDKYPHES  
QLPEEWENNRESLIVFMEQVHRGIKGLVRDSHGKGI PNAIISVEGINHDIRTANDGDYWRLL  
NPGEYVVTAKAEGFTASTKNCMVG YDMGATRCDFTL SKTNMARI REIMEKFGKQPVSLPARR  
LKLGRKRRRQRG

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FIGURE 37

CTAAGAGGACAAGATGAGGCCCGGCTCTCATTCTCTCCTAGCCCTTCTGTTCTTCTCTTGCC  
AAGCTGCAGGGGATTTGGGGGATGTGGGACCTCCAATTCCCAGCCCCGGCTTCAGCTCTTTC  
CCAGGTGTTGACTCCAGCTCCAGCTTCAGCTCCAGCTCCAGGTCCGGGCTCCAGCTCCAGCCG  
CAGCTTAGGCAGCGGAGGTTCTGTGTCCAGTTGTTTTCCAATTTACCGGCTCCGTGGATG  
ACCGTGGGACCTGCCAGTGCTCTGTTTCCCTGCCAGACACCACCTTTCCCGTGGACAGAGTG  
GAACGCTTGGAATTCACAGCTCATGTTCTTTCTCAGAAGTTTGAGAAAGAACTTTCTAAAGT  
GAGGGAATATGTCCAATTAATTAGTGTGTATGAAAAGAACTGTTAAACCTAACTGTCCGAA  
TTGACATCATGGAGAAGGATACCATTTCTTACACTGAACTGGACTTCGAGCTGATCAAGGTA  
GAAGTGAAGGAGATGGAAAACTGGTCATACAGCTGAAGGAGAGTTTTGGTGGAAGCTCAGA  
AATTGTTGACCAGCTGGAGGTGGAGATAAGAAATATGACTCTCTGGTAGAGAAGCTTGAGA  
CACTAGACAAAAACAATGTCCTTGCCATTGCGCGAGAAATCGTGGCTCTGAAGACCAAGCTG  
AAAGATGTTGAGGCCTCTAAAGATCAAAACACCCCTGTCTGCCACCTCCTCCCACTCCAGG  
GAGCTGTGGTCATGGTGGTGGTGAACATCAGCAAACCGTCTGTGGTTTCACTCAACTGGA  
GAGGTTTTTCTTATCTATATGGTGCTTGGGGTAGGGATTACTCTCCCAAGCATCCAAACAAA  
GGACTGTATTGGGTGGCGCCATTGAATACAGATGGGAGACTGTTGGAGTATTATAGACTGTA  
CAACACACTGGATGATTTGCTATTGTATATAAATGCTCGAGAGTTGCGGATCACCTATGGCC  
AAGGTAGTGGTACAGCAGTTTACAACAACAACATGTACGTCAACATGTACAACACCGGGAAT  
ATTGCCAGAGTTAACCTGACCACCAACACGATTGCTGTGACTCAAACCTCTCCCTAATGCTGC  
CTATAATAACCGCTTTTCATATGCTAATGTTGCTTGGCAAGATATTGACTTTGCTGTGGATG  
AGAATGGATTGTGGGTTATTTATTCAACTGAAGCCAGCACTGGTAACATGGTGATTAGTAAA  
CTCAATGACACCACACTTCAGGTGCTAAACACTTGGTATACCAAGCAGTATAAACCATCTGC  
TTCTAACGCCTTCATGGTATGTGGGGTTCTGTATGCCACCCGTAATGTAACACCAGAACAG  
AAGAGATTTTTTACTATTATGACACAAACACAGGGAAAGAGGGCAAACCTAGACATTGTAATG  
CATAAGATGCAGGAAAAAGTGCAGAGCATTAACCTATAACCCTTTTGACCAGAACTTTATGT  
CTATAACGATGGTTACCTTCTGAATTATGATCTTTCTGTCTTGCAGAAGCCCCAGTAAAGCTG  
TTTAGGAGTTAGGGTGAAAGAGAAAAATGTTTGTGAAAAAATAGTCTTCTCCACTTACTTAG  
ATATCTGCAGGGGTGTCTAAAAGTGTGTTTCAATTTTGAGCAATGTTTAGGTGCATAGTTCTA  
CCACACTAGAGATCTAGGACATTTGTCTTGATTTGGTGAGTTCTCTTGGGAATCATCTGCCT  
CTTCAGGCGCATTTTGAATAAAGTCTGTCTAGGGTGGGATTGTGAGAGTCTAGGGGCACT  
GTGGGCCTAGTGAAGCCTACTGTGAGGAGGCTTCACTAGAAGCCTTAAATTAGGAATTAAGG  
AACTTAAAACTCAGTATGGCGTCTAGGGATTCTTTGTACAGGAAATATTGCCCAATGACTAG  
TCCTCATCCATGTAGCACCCTAATTCTTCCATGCCTGGAAGAAACCTGGGGACTTAGTTAG  
GTAGATTAATATCTGGAGCTCCTCGAGGGACCAAATCTCCAACCTTTTTTTTCCCCTCACTAG  
CACCTGGAATGATGCTTTGTATGTGGCAGATAAGTAAATTTGGCATGCTTATATATTCTACA  
TCTGTAAAGTGTGAGTTTTATGGAGAGAGGCCTTTTTATGCATTAAATTGTACATGGCAA  
TAAATCCCAGAAGGATCTGTAGATGAGGCACCTGCTTTTTCTTTCTCTCATTGTCCACCTT  
ACTAAAAGTCAGTAGAATCTTCTACCTCATAACTTCCTTCCAAAGGCAGCTCAGAAGATTAG  
AACCAGACTTACTAACCAATCCACCCCCCACCACCCCTTCTACTGCCTACTTTAAAAAA  
ATTAATAGTTTTCTATGGAAGTGTCTAAGATTAGAAAAATTAATTTTCTTTAATTTCTTA  
TGGACTTTTATTATCATGACTCTAAGACTATAAGAAAATCTGATGGCAGTGACAAAGTGCTA  
GCATTTATTGTTATCTAATAAGACCTTGGAGCATATGTGCAACTTATGAGTGTATCAGTTG  
TTGCATGTAATTTTTGCCTTTGTTTAAAGCCTGGAACCTGTAAGAAAATGAAAATTTAATTTT  
TTTTTCTAGGACGAGCTATAGAAAAGCTATTGAGAGTATCTAGTTAATCAGTGCAGTAGTTG  
GAAACCTTGCTGGTGTATGTGATGTGCTTCTGTGCTTTTGAATGACTTTATCATCTAGTCTT  
TGTCTATTTTTCTTTGATGTTCAAGTCCTAGTCTATAGGATTGGCAGTTTAAATGCTTTAC  
TCCCCCTTTTAAATAAATGATTAAATGTGCTTTGAAAAAAAAAAAAAAAAAAAAAAAAAAAA

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FIGURE 38

MRPGLSFLLALLFFLGQAAGDLGDVGPPIPSPGFSSFPGVDSFFFSSSSSRSGSSSSSRSLGS  
GGSVSQLF SNFTGSVDDRGTCCQCSVSLPDTTFPVDRVERLEFTAHVLSQKFEKELSKVREYV  
QLISVYEKKLLNLTVRIDIMEKDTISYTELDFELIKVEVKEMEKLVIQLKESFGGSSEIVDQ  
LEVEIRNM TLLVEKLETLDKNNVLAIRREIVALKTKLKECEASKDQNTPVVHPPPTPGSCGH  
GGVVNISKPSVVQLNWRGFSYLYGAWGRDYSPQHFNKGLYWVAPLNTDGRLLLEYRLYNTLD  
DLLLLYNARELRITYGQSGTAVYNNNMVYVNMVNTGNIARVNLTNTIAVTQTLPNAAAYNNR  
FSYANVAWQDIDFAVDENGLWVIYSTEASTGNMVISKLNDTTLQVLNTWYTKQYKPSASNAF  
MVCGLVLYATRMTMNRTEEIFYYYDTNTGKEGKLDIVMHKMQEKVQSINYNPFDQKLYVYNDG  
YLLNYDLSVLQKPQ



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FIGURE 39

GCTCTGAAGACCAAGCTGAAAGAGTGTGAGGCCTCTAAAGATCAAACACCCCTGTGCTCCAC  
CCTCCTCCCACTCCAGGGAGCTGTGGTCATGGTGGTGTGGTGAACATCAGCAAACCGTCTGT  
GGTTCAGCTCAACTGGAGAGGGTTTTCTTATCTATATGGTGCTTGGGGTAGGGATTACTCTC  
CCCAGCATCCAAACAAAGGNATGTATTGGGNGGCGCCATTGAATACAGATGGGAGACTGTTG  
GAGTATTATAGACTGTACAACCCACTGGATGATTTGCTATTGTATATAAATGCTCGAGAGTT  
GCGGATCACCTATGGCCAAGGTAGTGGTACAGCAGTTTACAACAACAACATGTACGTCAACA  
TGTACAACACCGGNATATTGCCAGAGTTAACCTGACC

## FIGURE 40

TCTCGCAGATAGTAAATAATCTCGGAAAGGCGAGAAAGAAGCTGTCTCCATCTTGTCTGTAT  
CCGCTGCTCTTGTGACGTTGTGGAGATGGGGAGCGTCCTGGGGCTGTGCTCCATGGCGAGCT  
GGATACCATGTTTGTGTGGAAGTGCCCGTGTTTGTCTATGCCGATGCTGTCTTAGTGGAAC  
AACTCCACTGTAACTAGATTGATCTATGCACTTTTCTTGCTTGTGGAGTATGTGTAGCTTG  
TGTAATGTTGATACCAGGAATGGAAGAACAACCTGAATAAGATTCTGGATTTTGTGAGAATG  
AGAAAGGTGTTGTCCCTTGTAACTTTTGGTTGGCTATAAAGCTGTATATCGTTTGTGCTTT  
GGTTTGGCTATGTTCTATCTTCTTCTCTCTTTACTAATGATCAAAGTGAAGAGTAGCAGTGA  
TCCTAGAGCTGCAGTGCACAATGGATTTTGGTTCTTTAAATTTGCTGCAGCAATTGCAATTA  
TTATTGGGGCATTCTTCATTCCAGAAGGAACCTTTACAACCTGTGTGGTTTTATGTAGGCATG  
GCAGGTGCCTTTTGTTCATCCTCATACAACCTAGTCTTACTTATTGATTTTGCACATTATG  
GAATGAATCGTGGGTTGAAAAAATGGAAGAAGGGAACCTCGAGATGTTGGTATGCAGCCTTGT  
TATCAGCTACAGCTCTGAATTATCTGCTGTCTTTAGTTGCTATCGTCTGTCTTTTGTCTAC  
TACACTCATCCAGCCAGTTGTTTCAAGAAACAAGGCGTTTCACTAGTGTCAACATGCTCCTCTG  
CGTTGGTGCTTCTGTAATGTCTATACTGCCAAAAATCCAAGAATCACAACCAAGATCTGGTT  
TGTTACAGTCTTCAGTAATTACAGTCTACACAATGTATTTGACATGGTCAGCTATGACCAAT  
GAACCAGAAACAATTTGCAACCCCAAGTCTACTAAGCATAATTGGCTACAATACAACAAGCAC  
TGTCCCAAAGGAAGGGCAGTCAGTCCAGTGGTGGCATGCTCAAGGAATTATAGGACTAATTC  
TCTTTTTGTTGTGTGTATTTTATTCCAGCATCCGTACTTCAAACAATAGTCAGGTTAATAAA  
CTGACTCTAACAAGTGATGAATCTACATTAATAGAAGATGGTGGAGCTAGAAGTGATGGATC  
ACTGGAGGATGGGGACGATGTTTCAACGAGCTGTAGATAATGAAAGGGATGGTGTCACTTACA  
GTTATTCTTCTTTCACTTCATGCTTTTCTGGCTTCACTTTATATCATGATGACCTTTACC  
AACTGGTCCAGGTATGAACCTCTCGTGAGATGAAAAGTCAGTGGACAGCTGTCTGGGTGAA  
AATCTCTTCCAGTTGGATTGGCATCGTGTGTATGTTTGGACACTCGTGGCACCCTTGTTC  
TTACAAATCGTGATTTTGAAGTGAAGTGAAGTCTAGCATGAAAGTCCCCTTTGATTATTGC  
TTATTTGAAAACAGTATTTCCCACTTTTGTAAAGTTGTGTATGTTTTTGTCTCCCATGTAAC  
TTCTCCAGTGTTCTGGCATGAATTAGATTTTACTGCTTGTCAATTTTGTATTTTCTTACCAA  
GTGCATTGATATGTGAAGTAGAATGAATTGCAGAGGAAAGTTTTATGAATATGGTGATGAGT  
TAGTAAAGTGGCCATTATTGGGCTTATTCTCTGCTCTATAGTTGTGAAATGAAGAGTAAAA  
ACAAATTTGTTTGAATATTTTAAATTTATATTAGACCTTAAGCTGTTTTAGCAAGCATTAAA  
GCAAATGTATGGCTGCCTTTTGAATATTTGATGTGTTGCCTGGCAGGATACTGCAAGAAC  
ATGGTTTATTTTAAATTTTATAACAAGTCACTTAAATGCCAGTTGTCTGAAAAATCTTATA  
AGGTTTTACCCTTGATACGGAATTTACACAGGTAGGGAGTGTAGTGGACAATAGTGTAGGTTA  
TGGATGGAGGTGTCGGTACTAAATGAATAACGAGTAAATAATCTTACTTGGGTAGAGATGG  
CCTTTGCCAACAAAGTGAAGTGTGTTTGGTTGTTTTAACTCATGAAGTATGGGTTCACTGGA  
AATGTTTTGGAAGTCTGAAGGATTTAGACAAGGTTTTGAAAAGGATAATCATGGGTTAGAAGG  
AAGTGTGTTTGAAGTCACTTTGAAAGTTAGTTTTGGGCCAGCACGGTAGCTCACCTTGGT  
AATCCCAGCACTTTGGGAGCTTAAGTGGGTAGATTACTTGAGCCCAGGAATTGAGACCAGCT  
TGGCACATGGTGAACTGTTCTATAAAAAATAATCTGGCTTTGAGCATATGCCTGTGGTCCAG  
CACTGAGAGGCTAGTGAAGATTGCTGAGCCCAGAGCCAAAGGTTGCAGTGAGCAAGTCACGT  
CACTGCACTCTAGCTGGCACAGAGTAAGCCAAAAAATATATATATATTGAAATCAAGGAGG  
CAAAATTTTGAAGGGAAGGAAGTAAGTCAAAACCACTAGGCTTTAGTAGGTACTTATATA  
AAATCTAGTCCAGTTCTCTCATTTAAAAAATGAAGACACTGAAATACAGACTTAAATAGCT  
CAGATAGCTAATTAGGAAATTTCAAGTTGGCCAATAATAGCATTCTCTGACATTTAAAAA  
TAATTTCTATTCAAATAACATGCATATTGATTTACACCTCATACTGTGATAATTAATGTGAT  
GTGGATTGCTGGTGTCCAGCATGACCCATAAACAGGTGAGAAGAATGATGGAATGTTTTAGA  
ATAAACTCCTGCTTATAGTATACTACACAGTTCAAAGATGTTTAAATGCTTTTGTATTTA  
CTGCCATGTAATTGAAATATATAGATTATTGTAACCTTTCAACCTGAAATCAAGCAGTATG  
AGAGTTTAGTTATTGTATGTGTCACTAGTGTCTAATGAAGCTTTTAAATCTACAATTTCT  
TCTTTAAAAATATTTATTAATGTGAATGGAATATAACAATTCAGCTTAATTTCCCAACCTTA  
TTCTGTGTGTAGACATTGTATTCCACAATTTTGAATGGCTGTGTTTTACCTCTAAATAAATG  
AATTCAGAGAAAAA

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FIGURE 41

MGSVLGLCSMASWIPCLCGSAPCLLCRCCPSGNNSTVTRLIYALFLLVGVCVACVMLIPGME  
EQLNKIPGFCENEKGVVPCNILVGYSKAVYRLCFGLAMFYLLSLLMIKVKSSSDPRAAVHNG  
FWFFKFAAAIAIIIGAFFIPEGTFTTVWFYVGMAGAFCFILIQVLVIDFAHSWNESWVEKM  
EEGNSRCWYAALLSATALNYLLSLVAIVLFFVYYTHPASCSSENKAFISVNMLLCVGASVMSI  
LPKIQESQPRSGLLQSSVITVYTMYLTSAMTNEPETNCNPSLLSIIGYNTTSTVPKEGQSV  
QWWHAQGIIGLILFLLCVFYSSIRTSNNSQVNKLTLTSDESTLIEDGGARSDGSLEDGDDVH  
RAVDNERDGVITYSYSFFHFMFLASLYIMMTLTNWSRYEPSREMKSQWTAVVWKISSSWIGI  
VLYVWTLVAPLVLTNRDFD

FIGURE 42

GCGAGAAAGAAGCTGTCTCCATCTTGTCTGTATCCCGCTGCTTCTTGNGACGTTGTGGAGAT  
GGGGAGCGTCCCTGGGGCTGTGCTCCATGGCGAGCTGGATAACCATGTTTGTGTGGAAGTGCC  
CCGTGTTTGCTATGCCGATGCTGTCCTAGTGGAACAANTCCACTGTAACTAGATTGATCTA  
TGCACTTTTCTTGCTTGTTGGAGTATGTGTAGCTTGTGTAATGTTGATACCAGGAATGGAAG  
AACAACTGAATAAGATTCCTGGATTTTGTGAGAATGAGAAAGGTGTTGTCCCTTGTAACATT  
TTGGTTGGCTATAAAGCTGTATATCGTTTGTGCTTTGGTTTGGCTATGTTCTATCTTCTTCT  
CTCTTTACTAATGATCAAAGTGAAGAGTAGCAGTGATCCTAGAGCTGCAGTGCACAATGGAT  
TTTGGTTCTTTAAATTTGCTGCAGCAATTGCAATTATTATTGGGGC

FIGURE 43

GTTATTGTGAACTTTGTGGAGATGGGAGGTCNTGGGGCTGTGTTCCATGGCGAGCTGGATAC  
CANGTTTGTGTGGAAGTGCCCCGTGTTTGNTATGCCGATGCTGTCCTAGTGGAAACAANTCC  
ACTGTAATTAGATTGATNTATGCACTTTTNTTGCTTGTTGGAGTANGTGTAGCTTGTGTAAT  
GTTGATACCAGGAATGGAAGAACAACCTGAATAAGATTCCTGGATTTTGTGAGAATGAGAAAG  
GTGTTGTCCCTTGTAACATTTTGGTTGGCTATAAAGCTGTATATNGTTTGTGCTTTGGTTTG  
GCTANGTTCTATNTTCTTCTCTCTTTACTAATGATCAAAGTGAAGAGTAGCAGTGATCCTAG  
AGCTGCAGTGCACAATGGATTTTGGTTTTTTTAAATTTGCTGCAGCAATTGCAATTATTATTG  
GGGC

**FIGURE 44**

AAGAAGCTGTCTCCATCTTGTCTGTATCCGCTGCTCTTGTGAACGTTNTGGAGATGGGGAGC  
GTCCTTGGGGTTGCTCCATGGCGAGCTGGATAACCATGTTTGTGTGGAAAGTGCCCCGTGTT  
TGCTATGCCGATGCTGTCCCTAGTGGAACAACCTCCACTGTAACTAGATTGATCTATGCACTT  
TTCTTGCTTGTGGAGTATGTGTAGCTTGTGTAATGTTGATACCAGGAATGGAAGAACAACCT  
GAATAAGATTCTGGATTTTGTGAGAATGAGAAAGGTGTTGTCCCTTGTAACATTTTGGTTG  
GCTATAAAGCTGTATATCGTTTGTGCTTTGGTTTGGCTATGTTCTATCTTCTCTCTTTA  
CTAATGATCAAAGTGAAGAGTAGCAGTGATCCTAGAGCTGCAGTGCACAATGGATTTTGGTT  
CTTTAAATTTGCTGCAGCAATTGCAATTATTATTGGGGC

FIGURE 45

GCTGTCCTTAGTGGAACAANTCCAACCTGTAACCTGGATTGATCTATGCACTTTTTTCCTTG  
CTTGTTGGAGTATGTGTAGCTTTGTGTAATGTTGTTCCCAGGATTGGANGAACAACTGAATA  
AGATTCCCTGGATTTTTGTGAGAATGAGAAAGGTGTTGTCCCCTTGTAACATTTTTGGTTGGC  
TATAAAGCTGTATATCGTTTGTGCTTTGGTTTGGCTATGTTCTATCTTCTTCTCTTTACT  
AATGATCAAAGTGAAGAGTAGCAGTGATCCTAGAGCTGCAGTGCACAATGGATTTTTGGTTCT  
TTAAATTTGCTGCAGCAATTGCAATTATTATTGGGGCATTCTTCATTCCAGAAGGAACTTTT  
ACAACTGTGTGGTTTTATGTAGGCATGGCAGGTGCCTTTTGTTCATCCTCATACAACCTAGT  
CTTACTTATTGATTTTGCACATTCATGGAATGAATCGTGGGTGAAAAAATGGAAGAAGGGA  
ACTCGAGATGTTGGTATGCAGCCTTGTTATCAGCTACAGCTCTGAATTATCTGCTGTCTTTA  
GTTGCTATCGTCCTGTTCTTTGTCTACTACACTCATCCAGCCAGTTGTTTCAGAAAACAAGGC  
GTTTCATCAGTGTCAACATGCTCCTCTGCGTTGGTGCTTCTGTAATG

FIGURE 46A

CTCGGGCGCGCACAGGCAGCTCGGTTTGCCTGCGATTGAGCTGCGGGTTCGCGGCCGGCGCC  
GGCCTCTCCAATGGCAAATGTGTGTGGCTGGACGCGAGCGCGAGGCTTTCGGCAAAGGCAGT  
CGAGTGTTCAGACCGGGGCGAGTCCTGTGAAAGCAGATAAAAGAAAACATTTATTAACGT  
GTCATTACGAGGGGAGCGCCCGGGCGGGGCTGTGCGACTCCCCGCGGAACATTTGGCTCCCT  
CCAGCTCCGAGAGAGGAGAAGAAGAAAGCGGAAAAGAGGCAGATTCACGTGTTTTCCAGCCA  
AGTGGACCTGATCGATGGCCCTCCTGAATTTATCAGATATTTGATTATTAGCGATGCCCC  
CTGGTTTGTGTGTTACGCACACACAGTGCACACAAGGCTCTGGCTCGCTTCCCTCCCTCGT  
TTCCAGCTCCTGGGCGAATCCACATCTGTTTCAACTCTCCGCCGAGGGCGAGCAGGAGCGA  
GAGTGTGTGGAATCTGCGAGTGAAGAGGGACGAGGGAAAAGAAAACAAAGCCACAGACGCAAC  
TTGAGACTCCCGCATCCCAAAAGAAAGCACCAGATCAGCAAAAAAGAAAGATGGGCCCCCGA  
GCCTCGTGCTGTGCTTGCTGTCCGCAACTGTGTTCTCCCTGCTGGGTGGAAGCTCGGCCTTC  
CTGTGCGACCAACCGCTGAAAGGCAGGTTTCAGAGGGACCGCAGGAACATCCGCCCAACAT  
CATCCTGGTGCTGACGAGCAGCAGGATGTGGAGCTGGGTTCATGCAGGTGATGAACAAGA  
CCCGGCGCATCATGGAGCAGGGCGGGCGCACTTCATCAACGCCTTCGTGACCACACCCATG  
TGCTGCCCTCACGCTCCTCCATCCTCACTGGCAAGTACGTCCACAACCACAACACCTACAC  
CAACAATGAGAACTGCTCCTCGCCCTCCTGGCAGGCACAGCAGAGAGCCGCACCTTTGCCG  
TGTAACCTCAATAGCACTGGCTACCGACAGCTTTCTTCGGGAAGTATCTTAATGAATACAAC  
GGCTCCTACGTGCCACCCGGCTGGAAGGAGTGGGTCCGACTCCTTAAAAACTCCCGCTTTTA  
TAACTACACGCTGTGTGCGAACGGGGTGAAAGAGAAGCACGGCTCCGACTACTCCAAGGATT  
ACCTCACAGACCTCATACCAATGACAGCGTGAGCTTCTTCCGCACGTCCAAGAAGATGTAC  
CCGCACAGGCCAGTCTCATGGTCATCAGCCATGCAGCCCCCAGGGCCCTGAGGATTACAGC  
CCCACAATATTACGCCTCTTCCCAAACGCATCTCAGCACATCAGCCGAGCTACAACCTACG  
CGCCCAACCCGGACAAACACTGGATCATGCGCTACACGGGGCCCATGAAGCCCATCCACATG  
GAATTCACCAACATGCTCCAGCGGAAGCGCTTGACAGCCCTCATGTGCGGTGGACGACTCCAT  
GGAGACGATTTACAACATGCTGGTTGAGACGGGCGAGCTGGACAACACGTACATCGTATACA  
CCGCCGACCACGGTTACCACATCGGCCAGTTTGGCCCTGGTGAAAGGGAAATCCATGCCATAT  
GAGTTTGACATCAGGTTCCCGTTCTACGTGAGGGGCCCAACGTGGAAGCCGGTGTCTGAA  
TCCCCACATCGTCTCAACATTGACCTGGCCCCCACCATCCTGGACATTGCAGGCCTGGACA  
TACCTGCGGATATGGACGGGAAATCCATCCTCAAGCTGCTGGACACGGAGCGGCCGTGAAT  
CGGTTTTCACTTGAAAAAGAAGATGAGGGTCTGGCGGGACTCCTTCTTGTTGGAGAGAGGCAA  
GCTGCTACACAAGAGAGACAATGACAAGGTGGACGCCAGGAGGAGAACTTTCTGCCCAAGT  
ACCAGCGTGTGAAGGACCTGTGTGAGCGTGTGAGTACCAGACGGCGTGTGAGCAGCTGGGA  
CAGAAGTGGCAGTGTGTGGAGGACGCCACGGGGAAGCTGAAGCTGCATAAGTGCAAGGGCCC  
CATGCGGCTGGGCGGCAGCAGAGCCCTCTCCAACCTCGTGCCCAAGTACTACGGGCAGGGCA  
GCGAGGCCTGCACCTGTGACAGCGGGGACTACAAGCTCAGCCTGGCCGACGCGGGAACAAA  
CTCTTCAAGAAGAAGTACAAGGCCAGCTATGTCCGCAGTCGCTCCATCCGCTCAGTGGCCAT  
CGAGGTGGACGGCAGGGTGTACCACGTAGGCCTGGGTGATGCCGCCAGCCCCGAAACCTCA  
CCAAGCGGCACTGGCCAGGGGCCCTGAGGACCAAGATGACAAGGATGGTGGGGACTTCAGT  
GGCACTGGAGGCCTTCCCGACTACTCAGCCGCCAACCCATTAAAGTGACACATCGGTGCTA  
CATCCTAGAGAACGACACAGTCCAGTGTGACCTGGACCTGTACAAGTCCCTGCAGGCCTGGA  
AAGACCACAAGCTGCACATCGACCACGAGATTGAAACCCTGCAGAACAAAATTAAGAACCTG  
AGGGAAGTCCGAGGTACCTGAAGAAAAAGCGCCAGAAGAATGTGACTGTACAAAATCAG  
CTACCACACCCAGCACAAAGGCCGCTCAAGCACAGAGGCTCCAGTCTGCATCCTTTTCAGGA  
AGGGCCTGCAAGAGAAGGACAAGGTGTGGCTGTTGCGGGAGCAGAAGCGCAAGAAGAACTC  
CGCAAGCTGCTCAAGCGCCTGCAGAACAACGACAGTGCAGCATGCCAGGCCTCACGTGCTT  
CACCCACGACAACCAGCACTGGCAGACGGCGCCTTTCTGGACACTGGGGCCTTTCTGTGCCT  
GCACCAGCGCCAACAATAACACGTAAGTGGTGATGAGGACCATCAATGAGACTCACAATTC



FIGURE 46B

CTCTTCTGTGAATTTGCAACTGGCTTCCTAGAGTACTTTGATCTCAACACAGACCCCTACCA  
GCTGATGAATGCAGTGAACACACTGGACAGGGATGTCCTCAACCAGCTACACGTACAGCTCA  
TGGAGCTGAGGAGCTGCAAGGGTTACAAGCAGTGTAACCCCGGACTCGAAACATGGACCTG  
GATGGAGGAAGCTATGAGCAATACAGGCAGTTTCAGCGTCGAAAGTGGCCAGAAATGAAGAG  
ACCTTCTTCCAAATCACTGGGACAACTGTGGGAAGGCTGGGAAGGTTAAAGAAACAACAGAGG  
TGGACCTCCAAAAACATAGAGGCATCACCTGACTGCACAGGCAATGAAAAACCATGTGGGTG  
ATTTCCAGCAGACCTGTGCTATTGGCCAGGAGGCTGAGAAAGCAAGCACGCACTCTCAGTC  
AACATGACAGATTCTGGAGGATAACCAGCAGGAGCAGAGATAACTTCAGGAAGTCCATTTTT  
GCCCCTGCTTTTGCTTTGGATTATACCTCACCAGCTGCACAAAATGCATTTTTTCGTATCAA  
AAAGTCACCACTAACCCCTCCCCCAGAAGCTCACAAAGGAAAAACGGAGAGAGCGAGCGAGAGA  
GATTTCTTGGAATTTCTCCCAAGGGCGAAAGTCATTGGAATTTTAAATCATAGGGGAAA  
AGCAGTCCTGTTCTAAATCCTCTTATTCTTTTGGTTTGTACAAAGAAGGAACTAAGAAGCA  
GGACAGAGGCAACGTGGAGAGGCTGAAAACAGTGCAGAGACGTTTGACAATGAGTCAGTAGC  
ACAAAAGAGATGACATTTACCTAGCACTATAAACCCCTGGTTGCCTCTGAAGAACTGCCTTC  
ATTGTATATATGTGACTATTTACATGTAATCAACATGGGAACTTTTAGGGGAACCTAATAAG  
AAATCCCAATTTTCAGGAGTGGTGGTGTCAATAAACGCTCTGTGGCCAGTGTAAGAAAAA

FIGURE 47

MGPPSLVLCLLSATVFSLLGGSSAFLSHRLKGRFQDRRNIRPNIILVLTDDQDVELGSMQ  
VMNKTRRIMEQGGAHFINAFVTPMCCPSRSSILTGKYVHNHNTYTNNECSPSWQAQHE  
RTFAVYLNSTGYRTAFFGKYLNEYNGSYVPPGWKEWVGLLKNSRFYNYTLCRNGVKEKHGSD  
YSKDYLTDLITNDSVSFFRTSKKMYPHRPVLMVISHAAPHGPEDSAPQYSRLFPNASQHITP  
SYNYAPNPDKHWIMRYTGPMKPIHMEFTNMLQRKRLQTLMSVDDSMETIYNMLVETGELDNT  
YIVYTADHGYHIGQFGLVKGKSMPYEFDIRVPFYVRGPNVEAGCLNPHIVLNIDLAPTILDI  
AGLDIPADMKGKSIKLLDTERPVNRFHLKKKMRVWRDSFLVERGKLLHKRDNDKVDAQEEN  
FLPKYQRVKDLQCRAEYQTACEQLGQKWQCVEDATGKLKHLKCKGPMRLGGSRALSNLVPKY  
YGQGSEACTCDSGDYKLSLAGRRKKLFKKKYKASYVRSRSIRSVAI EVDGRVYHVGLGDAAQ  
PRNLTKRHWPGAPEDQDDKDGGDFSGTGGLPDYSAANPIKVTHRCYILENDTVQCDLDLYKS  
LQAWKDHKLHIDHEIETLQNKIKNLREVRGHLKKKRPEECDCHKISYHTQHKGRCLKHRGSSL  
HPFRKGLQEKDKVWLLREQKRKKLRKLLKRLQNNDTCSMPGLTCFTHDNQHWQTAPFWTLG  
PFCACTSANNNTYWC MRTINETHNFLFCEFATGFLEYFDLNTDPYQLMNAVNTLDRDVLNQL  
HVQLMELRSCKGYKQCNPRTRNMDLDGGSYEQYRQFQRRKWPEMKRPSSKSLGQLWEGWEG

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FIGURE 48

AACAAAGTTCAGTGACTGAGAGGGCTGAGCGGAGGCTGCTGAAGGGGAGAAAGGAGTGAGGA  
GCTGCTGGGCAGAGAGGGACTGTCCGGCTCCCAGATGCTGGGCCTCCTGGGGAGCACAGCCC  
TCGTGGGATGGATCACAGGTGCTGCTGTGGCGGTCTGTGCTGCTGCTGCTGCTGCTGGCCACC  
TGCCTTTTCCACGGACGGCAGGACTGTGACGTGGAGAGGAACCGTACAGCTGCAGGGGGAAA  
CCGAGTCCGCCGGGCCCCAGCCTTGGCCCTTCCGGCGGCGGGCCACCTGGGAATCTTTCACC  
ATCACCGTCATCCTGGCCACGTATCTCATGTGCCGAATGTGGGCCTCCACCACCACCACCAC  
CCCCGCCACACCCCTCACCACCTCCACCACCACCACCACCCCCACCGCCACCATCCCCGCCA  
CGCTCGCTTGAGGGCTGCTGTGCGCCGGTGCCCTGTGGACAGCAGCTGCCCCCTGCCCTCCCATCTG  
TTCCCAGGACAAGTGGACCCCATGTTTCCATGTGGAAGGATGCATCTCTGGGGTGAACGAGG  
GGAACAATAGACTGGGGCTTGCTCCAGCTGCATTTGCATGGCATGCCCCAGTGTACTATGGC  
AGCAGAGAATGGAGGAACACTGGGTCTGCAGTGCTGAAGGGTTTGGGGAGTGGAGAGCAAGG  
GTGCTCTTTCGGGGCTGGACAGCCCGTCTTGTGACAGTGAAGTCCCAGTGAGCCCCAGAAATG  
ACAAGCGTGCTTGGCAGAGCCAGCACACAAGTGGATGTGAAGTGCCCGTCTTGACCTCCTC  
ATCAGGCTGCTGCAGGCCTCTGGCGGGCAGGGCACTGGGAGAGGCCCTGAGAATGTCCTTTT  
GGTTTGGAGAAGGCAGTGTGAGGCTGCACAGTCAATTCATCGGTGCCTTAGTCCAAGAAAAT  
AAAAACCACTAAGAAGCTTTAAAAAAAAAAAAAAAAAAAAA

**FIGURE 49**

MLGLLGSTALVGWITGAAVAVLLLLLLLLLATCLFHGRQDCDVERNRTAAGGNRVRRAPWPFR  
RRGHLGIFHHHRHPGHVSHVFPNVGLHHHHHPRHTPHHLHHHHHPHRHHPRHAR

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FIGURE 50

GGCGGCTGCTGAGCTGCCTTGAGGTGCAGTGTTGGGGATCCAGAGCCATGTCGGACCTGCTA  
CTACTGGGCCTGATTGGGGCCCTGACTCTCTTACTGCTGCTGACGCTGCTGGCCTTTTGCCGG  
GTACTCAGGGCTACTGGCTGGGGTGGAAGTGAGTGCTGGGTACCCCCCATCCGCAACGTCA  
CTGTGGCCTACAAGTTCCACATGGGGCTCTATGGTGAGACTGGGCGGCTTTTCACTGAGAGC  
TGCAGCATCTCTCCCAAGCTCCGCTCCATCGCTGTCTACTATGACAACCCCCACATGGTGCC  
CCCTGATAAGTGCCGATGTGCCGTGGGCAGCATCCTGAGTGAAGGTGAGGAATCGCCCTCCC  
CTGAGCTCATCGACCTCTACCAGAAATTTGGCTTCAAGGTGTTCTCCTTCCCGGCACCCAGC  
CATGTGGTGACAGCCACCTTCCCCTACACCACCATTTCTGTCCATCTGGCTGGCTACCCGCCG  
TGTCCATCCTGCCTTGGACACCTACATCAAGGAGCGGAAGCTGTGTGCCTATCCTCGGCTGG  
AGATCTACCAGGAAGACCAGATCCATTTTCATGTGCCCCACTGGCACGGCAGGGAGACTTCTAT  
GTGCCCTGAGATGAAGGAGACAGAGTGGAATGGCGGGGGCTTGTGGAGGCCATTGACACCCA  
GGTGATGGCACAGGAGCTGACACAATGAGTGACACGAGTTCTGTAAGCTTGGAAAGTGAGCC  
CTGGCAGCCGGGAGACTTCAGCTGCCACACTGTACCTGGGGCGAGCAGCCGTGGCTGGGAT  
GACGGTGACACCCGAGCGAGCACAGCTACAGCGAGTCAGGTGCCAGCGGCTCCTCTTTTGA  
GGAGCTGGACTTGGAGGGCGAGGGGCCCTTAGGGGAGTCACGGCTGGACCTGGGACTGAGC  
CCCTGGGGACTACCAAGTGGCTCTGGGAGCCCACTGCCCCTGAGAAGGGCAAGGAGTAACCC  
ATGGCCTGCACCCCTCCTGCAGTGCAGTTGCTGAGGAACTGAGCAGACTCTCCAGCAGACTCT  
CCAGCCCTCTTCCTCCTTCTCTGGGGGAGGAGGGGTTCTGAGGGACCTGACTTCCCCTGC  
TCCAGGCCTCTTGCTAAGCCTTCTCCTCACTGCCCTTTAGGCTCCCAGGGCCAGAGGAGCCA  
GGGACTATTTTCTGCACCAGCCCCCAGGGCTGCCGCCCTGTTGTGTCTTTTTTTTCAGACTC  
ACAGTGGAGCTTCCAGGACCCAGAATAAAGCCAATGATTTACTTGTTTCACCTGGAAAAAAA  
AAAAAAAAA

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FIGURE 51

MSDLLLLGLIGGLTLLLLLTLLAFAGYSGLLAGVEVSAGSPPIRNVTVAYKFHMGLYGETGR  
LFTESCSISPKLRSIAVYYDNPHMVPPDKCRCVGSILSEGEESPSPELIDLYQKFGFKVFS  
FPAPSHVVTATFPYTTILSIWLATRRVHPALDTYIKERKLCAYPRLEIYQEDQIHFMCPAR  
QGDFYVPEMKETEWKWRGLVEAIDTQVDGTGADTMSDTSSVSLEVSPGSRETSAAATLSPGAS  
SRGWDDGDTRSEHSYSESGASGSSFEELDLEGEGLGESRLDPGTEPLGTTKWLWEPTAPEKGKE

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FIGURE 52

CCGCGGGAACGCTGTCCTGGCTGCCGCCACCCGAACAGCCTGTCCTGGTGCCCCGGCTCCCT  
GCCCCGCGCCAGTCATGACCCTGCGCCCTCACTCCTCCCGCTCCATCTGCTGCTGCTGCT  
GCTGCTCAGTGCGCGGTGTGCCGGGCTGAGGCTGGGCTCGAAACCGAAAGTCCCGTCCGGA  
CCCTCCAAGTGGAGACCCTGGTGGAGCCCCCAGAACCATGTGCCGAGCCCGCTGCTTTTGA  
GACACGCTTCACATACACTACACGGAAGCTTGGTAGATGGACGTATTATTGACACCTCCCT  
GACCAGAGACCCTCTGGTTATAGAACTTGGCCAAAAGCAGGTGATTCCAGGTCTGGAGCAGA  
GTCTTCTCGACATGTGTGTGGGAGAGAAGCGAAGGGCAATCATTCCTTCTCACTTGGCCTAT  
GGAAAACGGGGATTTCCACCATCTGTCCCAGCGGATGCAGTGGTGCAGTATGACGTGGAGCT  
GATTGCACTAATCCGAGCCAACTACTGGCTAAAGCTGGTGAAGGGCATTTCCTCTGGTAG  
GGATGGCCATGGTGCCAGCCCTCCTGGGCCTCATTGGGTATCACCTATACAGAAAGGCCAAT  
AGACCCAAAGTCTCCAAAAGAAGCTCAAGGAAGAGAAACGAAACAAGAGCAAAAAGAATA  
ATAAATAATAAATTTTAAAAAACTTAAAAAAAAAAAAAAAAAAAA

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**FIGURE 53**

MTLRPSLPLHL LLLLLLSAAVGRAEAGLETESPVRTLOVETLVEPPERCAEPAAFGDTLHI  
HYTGSLVDGRIIDTSLTRDPLVIELGQKQVIPGLEQSLLDMCVGEKRRAIIPSHLAYGKRGF  
PPSVPADAVVQYDVELIALIRANYWLKLVKGILPLVGMAMVPALLGLIGYHLYRKANRPKVS  
KKKLKEEKRNKSKKK



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FIGURE 54

CCCGGGAACGTGTTCCCTGGCTGCCGCACCCGAACAGCCTGTCCTGGTGCCCCGGCTCCCTGC  
CCCGCGCCAGTCATGACCCTGCGCCCCCTCACTCCTCCCGCTCCATCTGCTGCTGCTGCTGC  
TGCTCAGTGCGGCGGTGTGCCGGGCTGAGGCTGGGCTCGAAACCGAAAGTCCCGTCCGGACC  
CTCCAAGTGAGACCCCTGGTGGAGCCCCAGAACCATGTGCCGAGCCCGCTGCTTTTGGAGA  
CACGCTTCACATACACTACACGGGAAGCTTGGTAGATGGACGTATTATTGACACCTCCCTGA  
CCAGAGACCCTCTGGTTATAGAAGCTTGGCCAAAAGCAGGTGATTCCAGGTCTGGAGCAGAGT  
CTTCTCGACATGTGTGTGGGAGAGAAGCGAAGGGCAATCATTCCCTTCTCACTTGGCCTATGG  
AAAACGGGGATTTCCACCATCTGTCCCAGCGGATGCAGTGGTGCAGTATGACGTGGAGCTGA  
TTGCACTAATCCGAGCCAACTACTGGCTAAAGCTGGTGAAGGGCATTTTGCCTCTGGTAGGG  
ATGGCCATGGTGCCACCCTCCTGGGCCTCATTGGGTATCACCTATACAGAAAGGCCAATAGA  
CCCAAAGTCTCCAAAAAGAAGCTCAAGGAAGAGAAACGAAACAAGAGCAAAAAGAAATAATA  
AATAATAAATTTTAAAAAACTTA

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FIGURE 55

CCGAAAGTCCCGTCCGGACCCTCCAAGTGGAGACCCTGGTGGAGCCCCCAGAACCATGTGCC  
GAGCCCGCTGCTTTTGGAGACACGCTTCACATACACTACACGGGAAGCTTGGTAGATGGACG  
TATTATTGACACCTCCCTGACCAGAGACCCTCTGGTTATAGAACTTGGCCAAAAGCAGGTGA  
TTCCAGGTCTGGAGCAGAGTCTTCTCGACATGTGTGTGGGAGAGAAGCGAAGGGCAATCATT  
CCTTCTCACTTGGCCTATGGAAAACGGGGATTTCCACCATCTGTCCCAGCGGATGCAGTGGT  
GCAGTATGACGTGGAGCTGATTGCACTAATCCGAGCCAACACTGGCTAAAGCTGGTGAAGG  
GCATTTTGCCCTCTGGTAGGGATGGCCATGGTGCCAGCCCTCCTGGGCCTCATTGGGTATCAC  
CTATACAGAAAGGCCAATAGACCCAAAGTCTCCAAAAAGAAGCTCAAGGAAGAGAAACGAAA  
CAAGAGCAAAAAGAAATAATAAATAATAAATTTAAAAAACTTAAAA

CTGCTGCATCCGGGTGCTCTGGAGGCTGTGGCCGTTTTGTTTTCTTGGCTAAAAATCGGGGAG  
TGAGGCGGGCCGGCGCGGCGCACACCGGGCTCCGGAACCACTGCACGACGGGGCTGGACTG  
ACCTGAAAAAAATGCTCTGGATTTCTAGAGGGCTTGAGATGCTCAGAATGCATTGACTGGGGG  
GAAAAGCGCAATACTATTGCTTCCATTGCTGCTGGTGTACTATTTTTTACAGGCTGGTGGAT  
TATCATAGATGCAGCTGTTATTTATCCACCATGAAAGATTTC AACCACTCATACCATGCCT  
GTGGTGTTATAGCAACCATAGCCTTCCTAATGATTAATGCAGTATCGAATGGACAAGTCCGA  
GGTGATAGTTACAGTGAAGGTTGTCTGGGTCAAACAGGTGCTCGCATTTGGCTTTTCGTTGG  
TTTCATGTTGGCCTTTGGATCTCTGATTGCATCTATGTGGATTCTTTTTGGAGGTTATGTTG  
CTAAAGAAAAAGACATAGTATAACCTGGAATTGCTGTATTTTTCCAGAATGCCTTCATCTTT  
TTTGGAGGGCTGGTTTTTAAAGTTTGGCCGCACTGAAGACTTATGGCAGTGAACACATCTGAT  
TTCCACAGCACAACAGCCCTGCATGGGTTTGTGTTGTTTTTTTACTGCTCACTCCCAACCTT  
TTGTAATGCCATTTTCTAACTTATTTCTGAGTGTAGTCTCAGCTTAAAGTTGTGTAATACT  
AAAATCACGAGAACACCTAAACAACAACCAAAAATCTATTGTGGTATGCATTGATTAACTT  
ATAAAATGTTAGAGGAACTTTACATGAATAATTTTTGTCAAATTTTATCATGGTATAATT  
TGTA AAAAATAAAAAGAAATTACAAAAGAAATTATGGATTGTCAATGTAAGTATTTGTCATA  
TCTGAGGTCCAAAACCACAATGAAAGTGCTCTGAAGATTTAATGTGTTTATTCAAATGTGGT  
CTCTTCTGTGTCAAATGTTAAATGAAATATAAACATTTTTTAGTTTTTAAATATTCCGTGG  
TCAAAATTCTTCCTCACTATAATTGGTATTTACTTTTACCAAAAATTCTGTGAACATGTAAT  
GTA ACTGGCTTTTGGAGGTCTCCAAGGGGTGAGTGGACGTGTTGGAAGAGAGAAGCACCAT  
GGTCCAGCCACCAGGCTCCCTGTGTCCCTTCCATGGGAAGGTCTTCCGCTGTGCCTCTCATT  
CCAAGGGCAGGAAGATGTGACTCAGCCATGACACGTGGTCTGGTGGGATGCACAGTCACTC  
CACATCCACCACTG

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**FIGURE 57**

MSGFLEGLRCSECIDWGEKRNTIASIAAGVLFFGWIIIDA AVIYPTMKDFNHSYHACGVI  
ATIAFLMINAVSNGQVRGDSYSEGCLGQTGARIWLFVGFMLAFGSLIASMWILFGGYVAKEK  
DIVYPGIAVFFQNAFIFFGGLVFKFGRTEDLWQ

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FIGURE 58

TTCTTGGCTAAAATCGGGGGAGTGAGGCGGGCCGGCGCGGCGACACCGGGCTCCGGAACC  
ACTGCACGACGGGGCTGGACTGACCTGAAAAAATGTCTGGATTTCTAGAGGGCTTGAGATG  
CTCAGAATGCATTGACTGGGGGGAAAAGCGCAATACTATTGCTTCCATTGCTGCTGGTGTAC  
TATTTTTTACAGGCTGGTGGATTATCATAGATGCAGCTGTTATTTATCCCACCATGAAAGAT  
TTCAACCACTCATACCATGCCTGTGGTGTATAGCAACCATAGCCTTCCTAATGATTAATGC  
AGTATCGAATGGACAAGTCCGAGGTGATAGTTACAGTGAAGGTTGTCTGGGTCAAACAGGTG  
CTCGCATTTGGCTTTTCGTTGGTTTTATGTTGGCCTTTGGATCTCTGATTGCATCTATGTGG  
ATTCTTTTTTGGAGGTTATGTTGCTAAAGAAAAAGACATAGTATACCCTGGAATTGCTGTATT  
TTTCCAGAATGCCTTCATCTTTTTTGGAGGGCTGGTTTTTAAGTTTGGC

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FIGURE 59

TGGACGGACCTGAAAAAATGTTTGGATTNTAGAGGGNTTGAGATGTTCAGAATGCATGAC  
TGGGGGAAAAGCGCAAATACTATTGCTTCCATTGCTGCTGGTGTANTATTTTTTACAGGCTG  
GTGGATTATCATAGATGCAGNTGTTATTTATCCCACCATGAAAGATTTCAACCANTCATACC  
ATGCCTGTGGTGTTATAGCAACCATAGCCTTCNTAATGATTAATGCAGTATCGAATGGACAA  
GTCCGAGGTGATAGTTACAGTGAAGGTTGTTTGGGTCAAACAGGTGCTCGCATTGCGCTTTT  
CGTTGGTTTCATGTTGGCCTTTGGATCTCTGATTGCATCTATGTGGATTCTTTTTGGAGGTT  
ATGTTGCTAAAGAAAAAGACATAGTATACCCTGGAATTGNTGTATTTTTCCAGAATGCCTTC  
ATCTTTTTTGGAGGGCTGGTTTTTAAGTTTGGCCGCACTGAAGANTTATGGCAGTG

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FIGURE 60

GGACACGGGGTTCCGGACCAATGCANGACGGGGTGGANTGACCTGAAAAAATGTTTGGATT  
TTTAGAGGGCTTGAGATGNTCAGAATGCATTGACTGGGGGAAAAGCGCAATANTATTGCTTT  
CCATTGCTGCTGGTGTACTATTTTTTACAGGGTGGTGGATTATCATAGATGCAGCTGTTATT  
TATCCCACCATGAAAGATTTNAACCACTCATACCATGCCTGTGGTGTTATAGCAACCATAGC  
CTTCCTAATGATTAATGCAGTATCGAATGGACAAGTCCGAGGTGATAGTTACAGTGAAGGTT  
GTTTGGGTCAAACAGGTGNTCGCATTTGGCTTTTCGTTGGTTTCATGTTGGCCTTTGGATTT  
CTGATTGNATTCTATGCGGATTCTTCTTGGAGGTTATGTTGCTAAAGAAAAAGACATAGTAT  
ACCCTGGAATTNCTNTATTTTTCCAGAATGCC

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**FIGURE 61**

TAGAGGGCTTGAGATGCTCAGAATGCATTGACTGGGGGGAAAAGCGCAATANTATTGCTTCC  
ATTGNTGNTGGTGTANTATTTTTTTACAGGCTGGTGGATTATNATAGATGCAGCTGTTATTT  
ATCCCACCATGAAAGATTTNAACCANTCATACCATGCCTGTGGTGTTATAGCAACCATAGCC  
TTCCTAATGATTAATGCAGTATNGAATGGACAAGTCCGAGGTGATAGTTACAGTGAAGGTTG  
TTTGGGTCAAACAGGTGNTNGCATTGGCTTTTNGTTGGTTTCATGTTGGCCTTTGGATCTN  
TGATTGCATTTATGTGGATTNTTTTTGGAGGTTATGTTGCTAAAGNAAAAGACATAGTATAC  
CCTGT



FIGURE 62

GGGAGGCTGTGNCCGTTTTGTTTTN.TGGCTAAAATCGGGGGAGTGAGGCGGCCCGGCGCGG  
CGNGACACCGGGTTCCGGGAACCATTGCACGACGGGGTGGACTGACCTGAAAAAAATGTTTG  
GATTTNTAGAGGGCTTGAGATGCTCAGAATGCATTGACTGGGGGGAAAAGCGCAATACTATT  
GCTTCCATTGCTGCTGGTGTAATAATTTTACAGGCTGGTGGATTATCATAGATGCAGCTGT  
TATTTATCCCACCATGAAAGATTTCAACCACTCATACCATGCCTGTGGTGTATAGCAACCA  
TAGCCTTCCTAATGATTAATGCAGTATCGAATGGACAAGTCCGAGGTGATAGTTACAGTGAA  
GGTTGTCTGGGTCAAACAGGTGCTCGCATTTGGCTTTTCGTTGGTTTCATGTTGGCCTTTGG  
ATNTCTGATTGCATCTATGTGGATTCTTTTTGGAGGTTATGTTGCTAAAGAAAAAGACATAG  
TATACCTGGAATTGCTGTATTTTTCCAGAATGCCTTCATNTTTTTTGGAGGGCTG

FIGURE 63

CGACGCCGGCGTGATGTGGCTTCCGCTGGTGTGCTCCTGGCTGTGCTGCTGCTGGCCGTCC  
TCTGCAAAGTTTACTTGGGACTATTCTCTGGCAGCTCCCCGAATCCTTTCTCCGAAGATGTC  
AAACGGCCCCCAGCGCCCTGGTAACTGACAAGGAGGCCAGGAAGAAGGTTCTCAAAACAAGC  
TTTTTTCAGCCAACCAAGTGCCGGAGAAGCTGGATGTGGTGGTAATTGGCAGTGGCTTTGGGG  
GCCTGGCTGCAGCTGCAATTCTAGCTAAAGCTGGCAAGCGAGTCCTGGTGTGGAACAACAT  
ACCAAGGCAGGGGGCTGCTGTACATCCTTTGGAAAGAATGGCCTTGAATTTGACACAGGAAT  
CCATTACATTGGGCGTATGGAAGAGGGCAGCATTGGCCGTTTTATCTTGGACCAGATCACTG  
AAGGGCAGCTGGACTGGGCTCCCCTGTCTCTCCTTTTGGACATCATGGTACTGGAAGGGCCC  
AATGGCCGAAAGGAGTACCCCATGTACAGTGGAGAGAAAGCCTACATTACAGGGCCTCAAGGA  
GAAGTTTCCACAGGAGGAAGCTATCATTGACAAGTATATAAAGCTGGTTAAGGTGGTATCCA  
GTGGAGCCCCCTCATGCCATCCTGTTGAAATTCCTCCCATTGCCCCGTGGTTTCAGCTCCTCGAC  
AGGTGTGGGCTGCTGACTCGTTTTCTCTCCATTCTTCAAGCATCCACCCAGAGCCTGGCTGA  
GGTCTCTGCAGCAGCTGGGGGCTCCTCTGAGCTCCAGGCAGTACTCAGCTACATCTTCCCCA  
CTTACGGTGTCACCCCAACCAACAGTGCCTTTTTCATGCACGCCCTGCTGGTCAACCACTAC  
ATGAAAGGAGGCTTTTATCCCCGAGGGGGTTCCAGTGAAATTGCCTTCCACACCATCCCTGT  
GATTACAGCGGGCTGGGGGCGCTGTCTCACAAGGCCACTGTGCAGAGTGTGTTGCTGGACT  
CAGCTGGGAAAGCCTGTGGTGTGAGTGTGAAGAAGGGGCATGAGCTGGTGAACATCTATTGC  
CCCATCGTGGTCTCCAACGCAGGACTGTTCAACACCTATGAACACCTACTGCCCCGGGAACGC  
CCGCTGCCTGCCAGGTGTGAAGCAGCAACTGGGGACGGTGCGGCCCGCTTAGGCATGACCT  
CTGTTTTTCATCTGCTGCGAGGCACCAAGGAAGACCTGCATCTGCCGTCCACCAACTACTAT  
GTTTACTATGACACGGACATGGACCAGGCGATGGAGCGCTACGTCTCCATGCCAGGGAAGA  
GGCTGCGGAACACATCCCTCTTCTCTTCTCGCTTTCCCATCAGCCAAAGATCCGACCTGGG  
AGGACCGATTCCCAGGCCGGTCCACCATGATCATGCTCATACCCACTGCCTACGAGTGGTTT  
GAGGAGTGGCAGGCGGAGCTGAAGGGAAAGCGGGCAGTGACTATGAGACCTTCAAAAACCTC  
CTTTGTGGAAGCCTCTATGTGAGTGGTCTGAAACTGTTCCACAGCTGGAGGGGAAGGTGG  
AGAGTGTGACTGCAGGATCCCCACTCACCACAGTTCTATCTGGCTGCTCCCCAGGTGCC  
TGCTACGGGGCTGACCATGACCTGGGCCGCTGCACCCTTGTGTGATGGCCTCCTTGAGGGC  
CCAGAGCCCCATCCCCAACCTCTATCTGACAGGCCAGGATATCTTCACTGTGGACTGCTCG  
GGGCCCTGCAAGGTGCCCTGCTGTGACAGCAGCGCCATCCTGAAGCGGAACCTTGTACTCAGAC  
CTTAAGAACTTTGATTCTAGGATCCGGGCACAGAAGAAAAAGAATTAGTTCCATCAGGGAGG  
AGTCAGAGGAATTTGCCCAATGGCTGGGGCATCTCCCTTGACTTACCCATAATGTCTTTCTG  
CATTAGTTCCCTTGACGTATAAAGCACTCTAATTTGGTTCTGATGCCTGAAGAGAGGCCCTAG  
TTTAAATCACAATCCGAATCTGGGGCAATGGAATCACTGCTTCCAGCTGGGGCAGGTGAGA  
TCTTTACGCCCTTTTATAACATGCCATCCCTACTAATAGGATATTGACTTGGATAGCTTGATG  
TCTCATGACGAGCGGCGCTCTGCATCCCTCACCCTGCCTCCTAACTCAGTGATCAAAGCGA  
ATATTCCATCTGTGGATAGAACCCTGGCAGTGTGTGAGCTCAACCTGGTGGGTTCAGTTT  
TGTCCTGAGGCTTCTGCTCTCATTCAATTTAGTGCTACGCTGCACAGTTCTACACTGTCAAGG  
GAAAAGGGAGACTAATGAGGCTTAACTCAAAACCTGGGCGTGGTTTTGGTTGCCATTCCATA  
GGTTTGGAGAGCTCTAGATCTCTTTTGTGCTGGGTTCACTGGCTCTTACAGGGACAGGAAAT  
GCCTGTGTCTGGCCAGTGTGGTTCTGGAGCTTTGGGGTAACAGCAGGATCCATCAGTTAGTA  
GGGTGCATGTGAGATGATCATATCCAATTCATATGGAAGTCCCGGGTCTGTCTTCTTATCA  
TCGGGGTGGCAGCTGGTTCTCAATGTGCCAGCAGGACTCAGTACCTGAGCCTCAATCAAGC  
CTTATCCACCAAATACACAGGGAAGGGTGATGCAGGGAAGGGTGACATCAGGAGTCAGGGCA  
TGGACTGGTAAGATGAATACTTTGCTGGGCTGAAGCAGGCTGCAGGGCATTCCAGCCAAGGG  
CACAGCAGGGGACAGTGCAGGGAGGTGTGGGGTAAGGGAGGGGAAGTCACATCAGAAAAGGGA  
AAGCCACGGAATGTGTGTGAAGCCAGAAATGGCATTTCAGTTAATTAGCACATGTGAGGG  
TTAGACAGGTAGGTGAATGCAAGCTCAAGGTTTGGAAAAATGACTTTTTCAGTTATGTCTTTG  
GTATCAGACATACGAAAGGTCTCTTTGTAGTTCTGTGTTAATGTAAACATTAATAAATTTATTG  
ATTCCATTGCTTTAAAAA

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FIGURE 64

MWLPLVLLLAVALLLAVLCKVYLGLFSGSSPNPFSEDVKRPPAPLVTDKEARKKVLKQAFSAN  
QVPEKLDVVVIGSGFGGLAAAAILAKAGKRVLVLEQHTKAGGCCHTFGKNGLEFDTGIHYIG  
RMEEGSIGRFILDQITEGQLDWAPLSSPFDIMVLEGPNRKEYPMYSGEKAYIQGLKEKFPQ  
EEAIIIDKYIKLVKVVSSGAPHAILLKFLPLPVVQLLDRCGLLTRFSPFLQASTQSLAEVLQQ  
LGASSELQAVLSYIFPTYGVTPNHSAFSMHALLVNHYMKGGFYPRGGSSEIAFHTIPVIQRA  
GGAVLTKATVQSVLLDSAGKACGVSVKKGHELVNIYCPIVVSNAGLFNTYEHLLPGNARCLP  
GVKQQLGTVRPGLGMTSVFICLRGTKEDLHLPSTNYYVYYDTMDQAMERYVSMFREEAAEH  
IPLLFFAFPSAKDPTWEDRFPGRSTMIMLIPTAYEWFEWQAELKGKRGSDYETFKNSFVEA  
SMSVVLKLFPPQLEGKVESVTAGSPLTNQFYLAAPRGACYGADHDLGRLHPCVMASLRAQSPI  
PNLYLTGQDIFTGCLVGALQGALLCSSAILKRNLYSCLKNLDNRIRAQKKKN

[illegible]

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**FIGURE 66**

MRVRIGLTLLLCVLLSLASASSDEEGSQDESLDSKTTLTSDSVKDHTTAGRVVAGQIFLD  
SEESELESSIQEEEDSLK3QEGESVTEDISFLESPNPENKDYEEPKKVRKPALTAIEGTAHG  
EPCHFPPFLFLDKEYDECTSDGREDGRLWCATTYDYKADEKWGFCETEEEEAAKRRQMQAEMM  
YQTGMKILNGSNKKSQKREAYRYLQKAASMNHTKALERVSYALLFGDYLPQNIQAAREMF EK  
LTEEGSPKGQTALGFLYASGLGVNSSQAKALVYYTFGALGGNLI AHMVLVSRL

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FIGURE 67

CTTCCCAGCCCTGTGCCCCAAAGCACCTGGAGCATATAGCCTTGCAGAACTTCTACTTGCCT  
GCCTCCCTGCCTCTGGCCATGGCCTGCCGGTGCCTCAGCTTCCTTCTGATGGGGACCTTCCT  
GTCAGTTTCCCAGACAGTCCTGGCCCAGCTGGATGCACTGCTGGTCTTCCCAGGCCAAGTGG  
CTCAACTCTCCTGCACGCTCAGCCCCCAGCACGTCACCATCAGGGACTACGGTGTGTCTCTGG  
TACCAGCAGCGGGCAGGCAGTGCCCCCTCGATATCTCCTCTACTACCGCTCGGAGGAGGATCA  
CCACCGGCCTGCTGACATCCCCGATCGATTCTCGGCAGCCAAGGATGAGGCCCACAATGCCT  
GTGTCCTCACCATTAGTCCCGTGCAGCCTGAAGACGACGCGGATTACTACTGCTCTGTTGGC  
TACGGCTTTAGTCCCTAGGGGTGGGGTGTGAGATGGGTGCCTCCCCTCTGCCTCCCATTTCT  
GCCCCTGACCTTGGGTCCCTTTTAACTTTCTCTGAGCCTTGCTTCCCCTCTGTAAAATGGG  
TTAATAATATTCAACATGTCAACAAC

FIGURE 68

MACRCLSFLMGTFLSVSQTVLAQLDALLVFPQVAQLSCTLSPQHVTIRDYGVSWYQQRAG  
SAPRYLLYYRSEEDHHRPADIPDRFSAKDEAHNACVLTISPVPEDDADYYCSVGYGFS

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FIGURE 69

GCCGCCCCGCCCCGAGACCGGGCCCCGGGGCGCGGGGCGGCGGGATGCGGCGCCCCGGGGCGG  
 CGATGACCGCGGAGCGCACGCCGCGGGCCCCGCCCTGACCCCGCGCCCCCGCTGAGCCC  
 CCGCGCGAGGTCCGGACAGGCCGAGATGACGCGGAGCCCCCTGTTGCTGCTCCTGCTGCCGC  
 CGCTGCTGCTGGGGGCTTCCACCCGGCCGCGCGCGCGCGAGGCCCCCAAAGATGGCGGAC  
 AAGGTGGTCCACGGCAGGTGGCCCGGCTGGGCCGCACTGTGCGGCTGCAGTGCCCAAGTGA  
 GGGGAGACCCCGCGCGCTGACCATGTGGACCAAGGATGGCCGCACCATCCACAGCGGCTGGA  
 GCCGCTTCCGCGTGCTGCCGAGGGGCTGAAGGTGAAGCAGGTGGAGCGGGAGGATGCCGGC  
 GTGTACGTGTGCAAGGCCACCAACGGCTTCGGCAGCGCTGAGCGTCAACTACACCTTCGTCTG  
 GCTGGATGACATTAGCCAGGGAAGGAGAGCCTGGGGCCGACAGCTCCTCTGGGGGTCAAG  
 AGGACCCCGCCAGCCAGCAGTGGGCACGACCGCGCTTCACACAGCCCTCCAAGATGAGGCGC  
 CGGGTGATCGCACGGCCCCGTGGGTAGCTCCGTGCGGCTCAAGTGCGTGCCAGCGGGCACCC  
 TCGGCCCCGACATCAGTGGATGAAGGACGACAGGCCCTTGACGCGCCAGAGGCCGCTGAGC  
 CCAGGAAGAAGAAGTGGACACTGAGCCTGAAGAACCTGCGGCCGAGGACAGCGGCAAAATAC  
 ACCTGCCGCGTGTCGAACCGCGCGGGCGCCATCAACGCCACCTACAAGGTGGATGTGATCCA  
 GCGGACCCCGTTCCAAGCCCCGTGCTCACAGGCACGCAACCCGTGAACACGACCGTGACTTCG  
 GGGGACCACTCCTTCCAGTGCAAGGTGCGCAGCGACGTGAAGCCGGTGATCCAGTGGCTG  
 AAGCGCGTGGAGTACGGCGCCGAGGGCCGCCAACCTCCACCATCGATGTGGGCGCCAGAA  
 GTTTGTGGTGCTGCCACGGGTGACGTGTGGTCCGCGCCCGACGGCTCCTACCTCAATAAGC  
 TGCTCATCACCCGTGCCCGCCAGGACGATGCGGGCATGTACATCTGCCCTTGGCGCCAACACC  
 ATGGGCTACAGCTTCCGCAAGCGCCTTCCCTACCGTGCTGCCAGACCCAAAACCGCCAGGGCC  
 ACCTGTGGCCTCCTCGTCTCGGCCACTAGCCTGCCGTGGCCCGTGGTCATCGGCATCCAG  
 CCGGCGCTGTCTTCATCCTGGGCACCCCTGCTCCTGTGGCTTTGCCAGGCCCAGAAGAAGCCG  
 TGCACCCCCGCGCCTGCCCTTCCCTGCTGGGCACCGCCCGCGGGGACGGCCCCGACCCG  
 CAGCGGAGACAAGGACCTTCCCTCGTTGGCCGCGCCTCAGCGCTGGCCCTGGTGTGGGGCTGT  
 GTGAGGAGCATGGGTCTCCGGCAGCCCCCAGCACTTACTGGGCCCAGGCCAGTTGCTGGC  
 CCTAAGTTGTACCCCAAACCTCTACACAGACATCCACACACACACACACACACTCTCACAC  
 ACACTCACACGTGGAGGGCAAGGTCCACCAGCACATCCACTATCAGTGCTAGACGGCACCGT  
 ATCTGCAGTGGGCACGGGGGGGCGGCCAGACAGGCAGACTGGGAGGATGGAGGACGGAGCT  
 GCAGACGAAGGCAGGGGACCCATGGCGAGGAGGAATGGCCAGCACCCCAAGGCAGTCTGTGTG  
 TGAGGCATAGCCCTGGACACACACACACAGACACACACTACCTGGATGCATGTATGCAC  
 ACACATGCGCGCACACGTGCTCCCTGAAGGCACACGTACGCACACGCACATGCACAGATATG  
 CCGCCTGGGCACACAGATAAGCTGCCCAAATGCACGCACACGCACAGAGACATGCCAGAACA  
 TACAAGGACATGCTGCCTGAACATACACACGCACACCCATGCGCAGATGTGCTGCTGGACA  
 CACACACACACACGGATATGCTGTCTGGACACACACACAGTGCAGATATGGTATCCGGACACA  
 CACGTGCACAGATATGCTGCCTGGACACACAGATAATGCTGCCTTGACACACACATGCACGG  
 ATATTGCCTGGACACACACACACACACACGCGTGCACAGATATGCTGTCTGGACACGCACAC  
 ACATGCAGATATGCTGCCTGGACACACACTTCCAGACACACGTGCACAGGCGCAGATATGCT  
 GCCTGGACACACGCAGATATGCTGTCTAGTCAACACACACACGCAGACATGCTGTCCGGACAC  
 ACACACGCATGCACAGATATGCTGTCCGGACACACACACGCACGCAGATATGCTGCCTGGAC  
 ACACACACAGATAATGCTGCCTCAACACTCACACACGTGCAGATATTGCCTGGACACACACA  
 TGTGCACAGATATGCTGTCTGGACATGCACACACGTGCAGATATGCTGTCCGGATACACACG  
 CACGCACACATGCAGATATGCTGCCTGGGCACACACTTCCGGACACACATGCACACACAGGT  
 GCAGATATGCTGCCTGGACACACACACAGATAATGCTGCCTCAACACTCACACACGTGCAGA  
 TATTGCCTGGACACACACATGTGCACAGATATGCTGTCTGGACATGCACACACGTGCAGATA  
 TGCTGTCCGGATACACACGCACGCACACATGCAGATATGCTGCCTGGGCACACACTTCCGGA  
 CACACATGCACACACAGGTGCAGATATGCTGCCTGGACACACGCAGACTGACGTGCTTTTGG  
 GAGGGTGTGCCGTGAAGCCTGCAGTACGTGTGCCGTGAGGCTCATAGTTGATGAGGGACTTT  
 CCCTGCTCCACCGTCACTCCCCAACTCTGCCCGCCTCTGTCCCCGCCTCAGTCCCCGCCTC  
 CATCCCCGCTCTGTCCCCTGGCCTTGGCGGCTATTTTTGCCACCTGCCCTTGGGTGCCCAGG  
 AGTCCCCTACTGCTGTGGGCTGGGGTTGGGGGACAGCAGCCCCAAGCCTGAGAGGCTGGAG  
 CCCATGGCTAGTGGCTCATCCCCAGTGCACTTCTCCCCCTGACACAGAGAAGGGGCCCTGGTA  
 TTTATATTTAAGAAATGAAGATAATATTAATAATGATGGAAGGAAGACTGGGTGTCAGGGAC  
 TGTGGTCTCTCTGGGGCCCGGGACCCGCTGGTCTTTCAGCCATGCTGATGACCACACCCC  
 GTCCAGGCCAGACACCACCCCCACCCCACTGTGCTGGTGGCCCCAGATCTCTGTAATTTTA  
 TGTAGAGTTTGTAGCTGAAGCCCCGTATATTTAATTTATTTTGTAAACACAAAA



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FIGURE 70

MTPSPLLLLLLPPLLLGAFPPAAAARGPPKMADKVVPRQVARLGRTVRLQCPVEGDPPPLTM  
WTKDGRTIHSGWSRFRVLPQGLKVKQVEREDAGVYVCKATNGFGSLSVNYTLVVLDLSPGK  
ESLGPDSSSGQEDPASQQWARPRFTQPSKMRRRVIA RPVGSSVRLKCVASGHPRPDITWMK  
DDQALTRPEAAEPRKKKWTLSLKNLRPEDSGKYTCRVSNRAGAINATYKVDVIQRTRSKPVL  
TGTHPVNTTVDFGGTTSFQCKVRSDVKPVIQWLKRVEYGAEGRHNSTIDVGGQKFVVLPTGD  
VWSRPDGSYLNKLLITRARQDDAGMYICLGANTMGYSFRSAFLT VLPDPKPPGPPVASSSSA  
TSLPWPVVIGIPAGAVFILGTLLLWLCQAQKKPCTPAPAPPLPGHRPPGTARDRSGDKDLPS  
LAALSAGPGVGLCEEHGSPAAPQHLLGPGPVAGPKLYPKLYTDIHTHTHTSHHTSHSHVEGKV  
HQHIHYQC

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## FIGURE 71A

CCCAGCTGAGGAGCCCTGCTCAAGACACGGTCACTGGATCTGAGAACTTCCCAGGGGACCG  
 CATTCCAGAGTCAGTGACTCTGTGAAGCACCCACATCTACCTCTTGCCACGTTCCCACGGGC  
 TTGGGGGAAAGATGGTGGGGACCAAGGCCTGGGTGTTCTCCTTCTGGTCTGGAAGTCACA  
 TCTGTGTTGGGGAGACAGACGATGCTCACCAGTCAGTAAGAAGAGTCCAGCCTGGGAAGAA  
 GAACCCAGCATCTTTGCCAAGCCTGCCGACACCCTGGAGAGCCCTGGTGAGTGACAAACAT  
 GGTTCACATCGACTACCCAGGCGGGAAGGGCGACTATGAGCGGCTGGACGCCATTTCGCTTC  
 TACTATGGGGACCGTGATGTGCCGTGCCCTGCCGCTAGAGGCTCGGACCACTGTACAGCCTGT  
 ACCTGCGGCAGCACTGGCCAGGTGGTCCATGGTAGTCCCCGTGAGGGTTTCTGGTGCCCTCA  
 ACAGGGAGCAGCGGCCTGGCCAGAACTGCTCTAATTACACCGTACGCTTCTCTGCCACCA  
 GGATCCCTGCGCCGAGACACAGAGCGCATCTGGAGCCCATGGTCTCCCTGGAGCAAGTGCTC  
 AGCTGCCGTGTGGTCAGACTGGGGTCCAGACTCGCACACGCATTGCTTGGCAGAGATGGTGT  
 CGCTGTGCAGTGAGGCCAGCGAAGAGGGTCAGCACTGCATGGGCCAGGACTGTACAGCCTGT  
 GACCTGACCTGCCCAATGGGCCAGGTGAATGCTGACTGTGATGCCTGCATGTGCCAGGACTT  
 CATGCTTCATGGGGCTGTCTCCCTTCCCGAGGTGCCCCAGCCTCAGGGGCTGCTATCTACC  
 TCTGACCAAGACGCGGAAGCTGCTGACCCAGACAGACAGTGTGGGAGATTCCGAATCCCT  
 GGCTTGTGCCCTGATGGCAAAAGCATCCTGAAGATCACAAGGTCAAGTTTGCCCCCATTTGT  
 ACTCACAATGCCCAAGACTAGCCTGAAGGCAGCCACCATCAAGGCAGAGTTTGTGAGGGCAG  
 AGACTCCATACATGGTGATGAACCCCTGAGACAAAAGCACGGAGAGCTGGGCAGAGCGTGTCT  
 CTGTGCTGTAAGGCCACAGGGAAGCCCAGGCCAGACAAGTATTTTGGTATCATAATGACAC  
 ATTGCTGGATCCTTCCCTCTACAAGCATGAGAGCAAGCTGGTGCTGAGGAACTGCAGCAGC  
 ACCAGGCTGGGGAGTACTTTTGCAAGGCCAGAGTGATGCTGGGGCTGTGAAGTCCAAGGTT  
 GCCCAGCTGATTGTACAGCATCTGATGAGACTCCTTGCAACCCAGTTCCTGAGAGCTATCT  
 TATCCGGCTGCCCCATGATTGCTTTTCAGAATGCCACCAACTCCTTCTACTATGACGTGGGAC  
 GCTGCCCTGTTAAGACTTGTGTCAGGGCAGCAGGATAATGGGATCAGGTGCCGTGATGCTGTG  
 CAGAACTGCTGTGGCATCTCCAAGACAGAGGAAAGGGAGATCCAGTGCAGTGGCTACACGCT  
 ACCCACCAAGGTGGCCAAGGAGTGCAGTGCAGCGGTGTACGGAACTCGGAGCATCGTGC  
 GGGGCCGTGTGAGTGTGCTGACAATGGGGAGCCCATGCGCTTTGGCCATGTGTACATGGGG  
 AACAGCCGTGTAAGCATGACTGGCTACAAGGGCACTTTCACCTCCATGTCCCCCAGGACAC  
 TGAGAGGCTGGTGCTCACATTTGTGGACAGGCTGCAGAAGTTTGTCAACACCACCAAGTGC  
 TACCTTTCAACAAGAAGGGGAGTGCCGTGTTCCATGAAATCAAGATGCTTCGTGCGAAAGAG  
 CCCATCACTTTTGGGAAGCCATGGAGACCAACATCATCCCCCTGGGGGAAGTGCTTGGTGAAGA  
 CCCCATGGCTGAACTGGAGATTCCATCCAGGAGTTTCTACAGGCAGAATGGGGAGCCCTACA  
 TAGGAAAAGTGAAGGCCAGTGTGACCTTCTGGATCCCCGAATATTTCCACAGCCACAGCT  
 GCCCAGACTGACCTGAACTTCATCAATGACGAAGGAGACACTTTCCCCCTTCGGACGTATGG  
 CATGTTCTCTGTGGACTTCAGAGATGAGTCACTCAGAGCCACTTAATGCTGGCAAAGTGA  
 AGGTCCACCTTGACTCGACCCAGGTCAAGATGCCAGAGCACATATCCACAGTGAAACTCTGG  
 TCACTCAATCCAGACACAGGGCTGTGGGAGGAGGAAGGTGATTTCAAATTTGAAATCAAAG  
 GAGGAACAAAAGAGAAGACAGAACCTTCTGGTGGGCAACCTGGAGATTCTGTGAGAGGAGGC  
 TCTTTAACCTGGATGTTCTGAAAGCAGGCGGTGCTTTGTTAAGGTGAGGGCCTACCGGAGT  
 GAGAGGTTCTTGCTAGTGAGCAGATCCAGGGGTTGTGATCTCCGTGATTAACTGAGCC  
 TAGAATCTGGCTTCTGTGCCAACCCCTAGGGCCTGGGGCCGCTTTGACAGTGTCTACAGGCC  
 CCAACGGGGCCTGTGTGCTGCTTCTGTGATGACCAGTCCCCTGATGCCTACTCTGCCTAT  
 GTCTTGGCAAGCCTGGCTGGGGAGGAACTGCAAGCAGTGAGTCTTCTCTAAATTCACCCC  
 AAATGCAATTGGCGTCCCTCAGCCCTATCTCAACAAGCTCAACTACCGTCCGACCGACCATG  
 AGGATCCACGGGTTAAAAAAGACAGCTTTCCAGATTAGCATGGCCAAGCCAAGGCCAACTCA  
 GCTGAGGAGAGCAATGGGCCCATCTATGCCCTTTGAGAACCTCCGGGCATGTGAAGAGGCACC  
 ACCCAGTGACGCCACTTCCGGTTCTACCAGATTGAGGGGGATCGATATGACTACAACACAG  
 TCCCCCTCAACGAAGATGACCCTATGAGCTGGACTGAAGACTATCTGGCATGGTGCCAAAG  
 CCGATGGAATTCAGGGCCTGCTATATCAAGGTGAAGATTGTGGGGCCACTGGAAGTGAATGT  
 GCGATCCCGCAACATGGGGGGCACTCATCGGCGGACAGTGGGGAAGCTGTATGGAATCCGAG  
 ATGTGAGGAGCACTCGGGACAGGGACCAGCCCAATGTCTCAGCTGCCTGTCTGGAGTTCAAG  
 TGCAGTGGGATGCTCTATGATCAGGACCGTGTGGACCGCACCTGGTGAAGGTCATCCCCCA  
 GGGCAGCTGCCGTGAGCCAGTGTGAACCCCATGCTGCATGAGTACCTGGTCAACCACTTGC  
 CACTTGCACTCAACAACGACACCACTGAGTACACCATGCTGGCACCTTGGCACCTTGGGC  
 CACAATCTAGGCATCTACACTGTCACTGACCAGGACCTCGCACGGCCAAGGAGATCGCGCT  
 CGGCCGGTGTCTTGTGTCACATCCGATGGCTCCTCCAGAATCATGAAGAGCAATGTGGGAG  
 TAGCCCTCACCTTCAACTGTGTAGAGAGGCAAGTAGGCCGCCAGAGTGCTTCCAGTACCTC  
 CAAAGCACCCAGCCAGTCCCCTGCTGCAGGCACTGTCCAAGGAAGAGTGCCCTCGAGGAG  
 GCAGCAGCGAGCGAGCAGGGGTGGCCAGCGCCAGGGTGGAGTGGTGGCCTCTCTGAGATTTT

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FIGURE 71B

CTAGAGTTGCTCAACAGCCCCTGATCAACTAAAGTTTTGTGGTACTTCACCCCTCTTCTGCCCT  
CATTTCATGTGACAGCCATTGTGAGACTGATGCACAACTGTCACTTGGTTAATTTAAGCAC  
TTCTGTTTTTCGTGAATTTGCTTGTGTTTCTTCATGCCTTTACTTACTTTGTCCCATGCTA  
CTGATTGGCACGTGGCCCCCACAATGGCACAATAAAGCCCCCTTGTGAAACTGTTCTTTAAA  
TGAAACACAAGAAATTGGCCACTGGTAAACTCTGCAGCTTCAACTGTACTTCATTTAATGC  
CATTAAATGCAAATATACTTCCTCTTCTTTTGCATGGTTTTGCCACCTCTGCAATAGTGAT  
AATCTGATGCTGAAGATCAAATAACCAATATAAAGCATATTTCTTGGCCTTGCTCCACAGGA  
CATAGGCAAGCCTTGATCATAGTTCATACATATAAATGGTGGTGAAATAAAGAAATAAAACA  
CAATACTTTTACTTGAAATGTAAATAACTTATTTATTTCTTTGCTAAATTTGGAATTCTAGT  
GCACATTCAAAGTTAAGCTATTAAATATAGGGTGATCATAGTTCCTCTACCAAGTCTGGAAA  
GAACATCTCCTGGTATCCACAATTACACCAGGTTGCTAACTGTATTTGTACATTTCCCTTTG  
CATTCGCTTTTGTTCCTTGCTAGAAACCCAGTGTAGCCCAGGGCAGATGTCAATAAATGCATA  
CTCTGTATTTGAAAAAA

FIGURE 72

MVGTKAWVFSFLVLEVTSVLGRQTMLTQSVRRVQPGKKNPSIFAKPADTLESPGEWTTWFNI  
DYPGGKGDYERLDAIRFYYGDRVCARPLRLEARTTDWTPAGSTGQVVHGSPREGFWCLNREQ  
RPGQNCSNYTVRFLCPPGSLRRDTERIWSPPSPWSKCSAACGQTGVQTRTRICLAEMVSLCS  
EASEEGQHCHMGQDCTACDLTCPMGQVNADCDACMCQDFMLHGAVSLPGGAPASGAAYLLTK  
TPKLLTQTDSDGRFRI PGLCPDGKSILKITKVKFAPIVLTMPKTSLKAATIKAEFVRAETPY  
MVMNPETKARRAGQSVSLCCKATGKPRPDKYFWYHNDTLLDPSLYKHESKLVLRLKQLQHQA  
EYFCKAQSDAGAVKSKVAQLIVTASDETPCNPVPESYLIRLPHDCFQNAATNSFYDVGRCPV  
KTCAGQQDNGIRCRDAVQNC CGISKTEEREIQCSGYTLPTKVAKECSCQRCCTETRSIVRGRV  
SAADNGEPMRFGHVYMGNSRVSM TGYKGTFTLHVPQDTERLVLT FVDRLQKFVNTTKVLPFN  
KKGS AVFHEIKMLRRKEPITLEAMETNIIPLGEVVGEDPMAELEIPSR SFYRQNGEPYIGKV  
KASVTFLDPRNISTATAAQTDLNF INDEGDTFPLRTYGMFSVDFRDEVTSEPLNAGKVKVHL  
DSTQVKMPEHISTVKLWSLNPDTGLWEEEGDFKFENQRRNKREDRTFLVGNLEIRERRLFNL  
DVPESRRCFVKVRAYRSE RFLPSEQIQGVVISVINLEPRTGFLSNPRAWGRFDSVITGPNGA  
CVPAFCDDQSPDAYSAYVLASLAGEELQAVESSPKFNPNAIGVPQP YLNKLN YRRTDHEDPR  
VKKTAFQISMAKPRPN SAEESNGPIYAFENLRACEEAPPSAAHFRFYQIEGDRYDYNTVPFN  
EDDPMSWTE DYLA WWP KPMEFRACYIKVKIVGPLEVNVR SRNMGGTHRRTVGKLYGIRDVRS  
TRDRDQPNVSAACLEFKCSGMLYDQDRVDRTL VKVIPQGSRRASVNPMLHEYLVNHLPLAV  
NNDTSEYTMLAPLDPLGHNYGIYTVTDQDPRTAKEIALGRCFDGTSDGSSRIMKSNVGVALT  
FNCVERQVGRQSAFQYLQSTPAQSPAAGTVQGRVPSRRQQRASRGGRQGGVVASLRFPRVA  
QQPLIN

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FIGURE 73

CTGCAAGTTGTTAACGCCTAACACACAAGTATGTTAGGCTTCCACCAAAGTCTCTCAATATAC  
CTGAATACGCACAATATCTTAACTCTTCATATTTGGTTTTGGGATCTGCTTTGAGGTCCCAT  
CTTCATTTAAAAAAAATACAGAGACCTACCTACCCGTACGCATACATACATATGTGTATAT  
ATATGTAACTAGACAAAGATCGCAGATCATAAAGCAAGCTCTGCTTTAGTTTCCAAGAAGA  
TTACAAAGAATTTAGAGATGATTTTGTCAAGATCCCTGTGATTATGCCCCTTTGGGTTACG  
GTGTCTCTCAGTGATGCAGCCCTACCCCTTTGGTTTGGGGACATTATGATTTGTGTAAAGACTCA  
GATTTACACGGAAGAAGGGAAAGTTTGGGATTACATGGCCTGCCAGCCGGAATCCACGGACA  
TGACAAAATATCTGAAAGTGAACTCGATCCTCCGGATATTACCTGTGGAGACCCTCCTGAG  
ACGTTCTGTGCAATGGGCAATCCCTACATGTGCAATAATGAGTGTGATGCGAGTACCCTGA  
GCTGGCACACCCCCCTGAGCTGATGTTTGATTTTGAAGGAAGACATCCCTCCACATTTTGGC  
AGTCTGCCACTTTGGAAGGAGTATCCCAAGCCTCTCCAGGTTAACATCACTCTGTCTTGGAGC  
AAAACCATTGAGCTAACAGACAACATAGTTTATTACCTTTGAATCTGGGCGTCCAGACCAAAT  
GATCCTGGAGAAGTCTCTCGATTATGGACGAACATGGCAGCCCTATCAGTATTATGCCACAG  
ACTGCTTAGATGCTTTTTCACATGGATCCTAAATCCGTGAAGGATTTATCACAGCATACGGTC  
TTAGAAATCATTTGCAAGAAGAGTACTCAACAGGGTATACAACAAATAGCAAAATAATCCA  
CTTTGAAATCAAAGACAGGTTTCGCGCTTTTGTCTGGACCTCGCCTACGCAATATGGCTTCCC  
TCTACGGACAGCTGGATACAACCAAGAACTCAGAGATTTCTTTACAGTCACAGACCTGAGG  
ATAAGGCTGTTAAGACCAGCCGTGGGGAAATATTTGTAGATGAGCTACACTTGGCAGCCTA  
CTTTTACGCGATCTCAGACATAAAGGTGCGAGGAAGGTGCAAGTGAATCTCCATGCCACTG  
TATGTTGTATGACAACAGCAAATTGACATGCGAATGTGAGCACAACACTACAGTCCAGAC  
TGTGGGAAATGCAAGAAGAATTATCAGGGCCGACCTTGGAGTCCAGGCTCCTATCTCCCAT  
CCCCAAAGGCACTGCAAATACCTGTATCCCCAGTATTTCCAGTATTGGTACGAATGTCTGCG  
ACAAAGAGCTCCTGCACTGCCAGAACGGAGGGACGTGCCACAACAACGTGCGCTGCGCTGTGC  
CCGGCCGCATACACGGGCATCCTCTGCGAGAAGCTGCGGTGCGAGGAGGCTGGCAGCTGCGG  
CTCCGACTCTGGCCAGGGCGCGCCCCCGCACGGCACCCACGCGCTGCTGCTGTGACCACGC  
TGCTGGGAACCGCCAGCCCCCTGGTGTCTAGGTGTACCTCCAGCCACACCGGACGGGCCCT  
GTGCCGTGGGGAAGCAGACACAACCCAAACATTTTGCTACTAACATAGGAAACACACATAC  
AGACACCCCCACTCAGACAGTGTACAACTAAGAAGGCCTAACTGAACTAAGCCATATTTAT  
CACCCGTGGACAGCACATCCGAGTCAAGACTGTTAATTTCTGACTCCAGAGGAGTTGGCAGC  
TGTTGATATTATCACTGCAAATCACATTGCCAGCTGCAGAGCATATTGTGGATTGGAAAGGC  
TGCGACAGCCCCCAAACAGGAAAGACAAAAACAAACAAATCAACCGACCTAAAAACATTG  
GCTACTCTAGCGTGGTGGCCCTAGTACGACTCCGCCCAGTGTGTGGACCAACCAATAGCA  
TTCTTTGCTGTGAGGTGCATTGTGGGCATAAGGAAATCTGTTACAAGCTGCCATATTGGCCT  
GCTTCCGTCCCTGAATCCCTTCCAACCTGTGCTTTAGTGAACGTTGCTCTGTAAACCTCGTT  
GGTTGAAAGATTTCTTTGTCTGATGTTAGTGATGCACATGTGTAACAGCCCCCTCTAAAAGC  
GCAAGCCAGTCATACCCCTGTATATCTTAGCAGCACTGAGTCCAGTGCAGACACACCCAC  
TATACAAGAGTGGCTATAGGAAAAAAGAAAGTGTATCTATCCTTTTGTATTCAAATGAAGTT  
ATTTTCTTGAACTACTGTAATATGTAGATTTTTTGTATTATTGCCAATTTGTGTTACCAGA  
CAATCTGTTAATGTATCTAATTGCAATCAGCAAAGACTGACATTTTATTTTGTCCCTCTTTG  
TTCTGTTTTGTTTTCACTGTGCAGAGATTTCTCTGTAAGGGCAACGAACGTGCTGGCATCAAA  
GAATATCAGTTTACATATATAACAAGTGAATAAGATTCCACCAAAGGACATTCTAAATGTT  
TTCTTGTGCTTTTAACTGGAAGATTTAAAGAATAAAAACTCCTGCATAAACGATTTTCAGG  
AATTTGTATTGCAATTTCTTAAGATGAAAGGAACAGCCACCAAGCAGTTTCACACTCACTTT  
ACTGATTTCTGTGTGGACTGAGTACATTCAGCTGACGAATTTAGTTCACAGGAAGATGGATT  
GATGTTCACTAGCTTGGACAACCTCTGCAAAATATGAGACTATTTCCACTTGGGAAAAATTA  
CAACAGCAAAAAAAAAAAAAAAAAAAAAA

FIGURE 74

MYLSRSLSIHALWVTVSSVMQPYPLVWGHYDLCKTQIYTEEGKVWDYMACQPESTDMTKYLK  
VKLDPPDITCGDPPETFCAMGNPYMCNNECDASTPELAHPPELMFD FEGRHPSTFWQSATWK  
EYPKPLQVNITLSWSKTIELTDNIVITFESGRPDQMILEKSLDYGRTWQPYQYYATDCLDAF  
HMDPKSVKDLSQHTVLEI ICTEEYSTGYTTNSKIIHFEIKDRFALFAGPRLRNMASLYGQLD  
TTKKLRDFFTVTDLRIRLLRPAVGEIFVDELHLARYFYAISDIKVRGRCKCNLHATVCVYDN  
SKLTCECEHNTTGPDCGKCKKNYQGRPWSPGSYLP I PKGTANTCIPSISSIGTNVCDNELLH  
CQNGGTCHNNVRCLCPAAYTGILCEKLRCEEAGSCGSDSGQGAPPHGTPALLLLTTLLGTAS  
PLVF

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FIGURE 75

CCCACGCGTCCGGGTGACCTGGGCCGAGCCCTCCCGGTCCGGCTAAGATTGCTGAGGAGGCGG  
CGGGTAGCTGGCAGGCGCCGACTTCCGAAGGCCGCCGTCCGGGCGAGGTGTCCTCATGACTT  
CTCTTGTGGACCATGTCCGTGATCTTTTTTGCCTGCGTGGTACGGGTAAGGGATGGACTGCC  
CCTCTCAGCCTCTACTGATTTTTTACCACACCCAAGATTTTTTGGGAATGGAGGAGACGGCTCA  
AGAGTTTAGCCTTGCGACTGGCCCAGTATCCAGGTGAGGTTCTGCAGAAGGTTGTGACTTT  
AGTATACATTTTTCTTCTTTTCGGGGACGTGGCCTGCATGGCTATCTGCTCCTGCCAGTGTCC  
AGCAGCCATGGCCTTCTGCTTCCTGGAGACCTGTGGTGGGAATTCACAGCTTCCTATGACA  
CTACCTGCATTGGCCTAGCCTCCAGGCCATACGCTTTTTCTTGAGTTTGACAGCATCATTAG  
AAAGTGAAGTGGCATTTTAACTATGTAAGTTCCTCTCAGATGGAGTGCAGCTTGAAAAAAT  
TCAGGAGGAGCTCAAGTTGCAGCCTCCAGCGGTTCTCACTCTGGAGGACACAGATGTGGCAA  
ATGGGGTGATGAATGGTCACACACCGATGCACTTGGAGCCTGCTCCTAATTTCCGAATGGAA  
CCAGTGACAGCCCTGGGTATCCTCTCCCTCATTCTCAACATCATGTGTGCTGCCCTGAATCT  
CATTGAGGAGTTCACCTTGCAGAACATTCTTTACAGGATCCAAGGAGCTGGTTCTGCTGGT  
TGGACCAAACCTCGTGAGCCAGCCACCCCTGACCCAAATGAGGAGAGCTCTGATTCTCCCAT  
CCGGGAGCAGTGATGTCAAACCTTCTGCTGCTGGGGAAATCTCATCAGCAGGGAGCCTGTGGA  
AAAGGGCATGTGAGTGAATCTGGGAATGGCTGGATTTCGGAAACATCTGCCCATGTGTATTG  
ATGGCAGAGCTGTTGCCCACAAGCGCCTTTTATTTAGGGTAAAATTAACAAATCCATTCTAT  
TCCTCTGACCCATGCTTAGTACATATGACCTTTAACCCTTACATTTATATGATTCTGGGGTT  
GCTTCAGAAGTGTTATTTTCATGAATCATTCATATGATTTGATCCCCAGGATTCTATTTTGT  
TTAATGGGCTTTTCTACTAAAAGCATAAAATACTGAGGCTGATTTAGTCAGGGCAAAACCAT  
TTACTTTACATATTCGTTTTCAATACTTGCTGTTTCATGTTACACAAGCTTCTTACGGTTTTTC  
TTGTAACAATAAAATATTTTGAGTAAATAATGGGTACATTTTAACAAACTCAGTAGTACAACC  
TAAACTTGTATAAAAGTGTTGTAATAATGTATAGCCATTTATATCCTATGTATAAATTAAATG  
AGGTGGCTTCAGAAATGGCAGAATAAATCTAAAGTGTTATTAAAAAATAAAAAAAAAAAAAA  
AAAAG

**FIGURE 76**

MSVIFACVVRVVDGLPLSASTDFYHTQDFLEWRRRLKSLALRLAQYPGRGSAEGCDFSIHF  
SSFGDVACMAICSCQCPAAMAFCFLETLWWEFTASYDTTCIGLASRPYAFLEFDSIIQVKW  
HFNYVSSSQMECSLEKIQEELKLQPPAVLTLEDTDVANGVMNGHTPMHLEPAPNFRMEPVTA  
LGILSLILNIMCAALNLIRGVHLAEHSLQDPRSWFCWLDQTS



FIGURE 77

TGCTTCCTGGAGACCCTGTGGTGGGAATTCACAGCTTCNTATGACACTACCTGCATTGGCNT  
AGCCTCCAGGCCATACGCCTTTCTTGAGTTTGACAGCATCATTGAGAAAGTGAAGTGGCATT  
TTAACTATGTAAGTTCCTNTCAGATGGAGTGCAGCTTGGAAAAAATTCAGGAGGAGCTCAAG  
TTGCAGCCTCCAGCGGTTCTCANTATGGAGGACACAGATGTGGCAAATGGGGT

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FIGURE 78

CTCAGCGGCGCTTCCTCGTAGCGAGCCTAGTGGCGGGTGTTTGCATTGAAACGTGAGCGCGA  
CCCGACCTTAAAGAGTGGGGAGCAAAGGGAGGACAGAGCCCTTTAAACGAGGCGGGTGGTG  
CCTGCCCCCTTTAAGGGCGGGGCGTCCGGACGACTGTATCTGAGCCCCAGACTGCCCCGAGTT  
TCTGTGCGAGGCTGCGAGGAAAGGCCCTAGGCTGGGTCTGGGTGCTTGGCGGCGGCGGCTT  
CCTCCCCGCTCGTCCTCCCCGGGCCCCAGAGGCACCTCGGCTTCAGTCATGCTGAGCAGAGTA  
TGGGAAGCACCTGACTACGAAGTGCTATCCGTGCGAGAACAGCTATTCCACGAGAGGATCCGC  
GAGTGTATTATATCAACACTTCTGTTTGCAACACTGTACATCCTCTGCCACATCTTCTTGAC  
CCGCTTCAAGAAGCCTGCTGAGTTCACCACAGTGGATGATGAAGATGCCACCGTCAACAAGA  
TTGCGCTCGAGCTGTGCACCTTTACCCTGGCAATTGCCCTGGGTGCTGTCTGCTCCTGCC  
TTCTCCATCATCAGCAATGAGGTGCTGCTCTCCCTGCCTCGGAACACTACTACATCCAGTGGCT  
CAACGGCTCCCTCATCCATGGCCTCTGGAACCTTGTTTTCTCTTCCCCAACCTGTCCCTCA  
TCTTCTCATGCCCTTTGCATATTTCTTCACTGAGTCTGAGGGCTTTGCTGGCTCCAGAAAG  
GGTGTCTGGGCGGGTCTATGAGACAGTGGTGATGTTGATGCTCCTCACTCTGCTGGTGCT  
AGGTATGGTGTGGGTGGCATCAGCCATTGTGGACAAGAACAAGGCCAACAGAGAGTCACTCT  
ATGACTTTTGGGAGTACTATCTCCCTACCTCTACTCATGCATCTCCTTCTTGGGGTTCTG  
CTGCTCCTGGTGTGTACTCCACTGGGTCTCGCCCGCATGTTCTCCGTCACTGGGAAGCTGCT  
AGTCAAGCCCCGGCTGCTGGAAGACCTGGAGGAGCAGCTGTACTGCTCAGCCTTTGAGGAGG  
CAGCCCTGACCCGAGGATCTGTAATCCTACTTCTCTGCTGGCTGCCTTTAGACATGGAGCTG  
CTACACAGACAGGTCTGGCTCTGCAGACACAGAGGGTCTGCTGGAGAAGAGGCGGAAGGC  
TTCAGCCTGGCAACGGAACCTGGGCTACCCCTGGCTATGCTGTGCTTGTGCTGCTGACGG  
GCCTGTCTGTGCTCATTGTGGCCATCCACATCCTGGAGCTGCTCATCGATGAGGCTGCCATG  
CCCCGAGGCATGCAGGGTACCTCCTTAGGCCAGGTCTCCTTCTCCAAGCTGGGCTCCTTTGG  
TGCCGTCAATTCAGGTTGTACTCATCTTTTACCTAATGGTGTCTCAGTTGTGGGCTTCTATA  
GCTCTCCACTCTTCCGGAGCCTGCGGCCCAGATGGCACGACACTGCCATGACGCAGATAATT  
GGGAAGTGTGTCTGTCTCCTGGTCCTAAGCTCAGCACTTCCTGTCTTCTCTCGAACCCTGGG  
GCTCACTCGCTTTGACCTGCTGGGTGACTTTGGACGCTTCAACTGGCTGGGCAATTTCTACA  
TTGTGTTCTCTACAACGCAGCCTTTGCAGGCCTCACCACACTCTGTCTGGTGAAGACCTTC  
ACTGCAGCTGTGCGGGCAGAGCTGATCCGGGCCTTTGGGCTGGACAGACTGCCGCTGCCCGT  
CTCCGGTTTCCCCCAGGCATCTAGGAAGACCCAGCACCAGTGAACCTCCAGCTGGGGGTGGGA  
AGGAAAAAACTGGACACTGCCATCTGCTGCCTAGGCCTGGAGGGAAGCCCAAGGCTACTTGG  
ACCTCAGGACCTGGAATCTGAGAGGGTGGGTGGCAGAGGGGAGCAGAGCCATCTGCACTATT  
GCATAATCTGAGCCAGAGTTTGGGACCAGGACCTCCTGCTTTTCCATACTTAACTGTGGCCT  
CAGCATGGGGTAGGGCTGGGTGACTGGGTCTAGCCCCCTGATCCCAAATCTGTTTACACATCA  
ATCTGCCTCACTGCTGTTCTGGGCCATCCCCATAGCCATGTTTACATGATTTGATGTGCAAT  
AGGGTGGGGTAGGGGCAGGGAAGGACTGGGCCAGGGCAGGCTCGGGAGATAGATTGTCTCC  
CTTGCTCTGGCCCAGCAGAGCCTAAGCACTGTGCTATCCTGGAGGGGCTTTGGACCACCTG  
AAAGACCAAGGGGATAGGGAGGAGGAGGCTTCAGCCATCAGCAATAAAGTTGATCCCAGGGA  
AAAAAA

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FIGURE 79

MEAPDYEVLSVREQLFHERIRECIISTLLFATLYILCHIIFLTRFKKPAEFTTVDDDEDATVVK  
IALELCTFTLAIALGAVLLLPPFSIISNEVLLSLPRNYITQWLNGSLIHGLWNLVFLFPNLSL  
IFLMPFAYFFTESEGFAGSRKGVLRVYETVVMLMLLTLLVLGMVWVASAIVDKNKANRESL  
YDFWEYYLPYLYSCISFLGVLLLLVCTPLGLARMFSVTGKLLVKPRLLEDLEEQLYCSAFEE  
AALTRRICNPTSCWLPDME LLHRQVLALQTQRV LLEKRRKASAWQRNLGYPLAMLCLLVLT  
GLSVLIVAIHILELLIDEAAMP RGMQGTSLGQVSFSKLGSGGAVIQVVLIFYLMVSSVVG FY  
SSPLFRSLRPRWHD TMTQIIGNCVCLLV LSSALPVFSRTLGLTRFDLLGDFGRFNWLG N FY  
IVFLYNAAFAGLTTLCLVKTF TAAVRAELIRAFGLDRLPLPVSGFPQASRKTQH Q

**FIGURE 80**

GGCTGCCGAGGGAAGGCCCTTGGGTTGGTCTTGGTTGCTTGGCGGCGGCGGNTTCNTCCCC  
~~GCTCGTCCTCCCCGGGCCCCAGAGGGCACCTEGGCTTCAGTCATGCTGAGCAGAGTATGGAAGC~~  
ACCTGACTACGAAGTGCTATCCGTGCGAGAACAGCTATTCCACGAGAGGATCCGCGAGTGTA  
TTATATCAACACTTCTGTTTGCAACACTGTACATCCTCTGCCACATCTTCCTGACCCGCTTC  
AAGAAGCCTGCTGAGTTCACCACAGTGGATGATGAAGATGCCACCG

FIGURE 81

GACCGACCTTAAAGAGTGGGAGCAAAGGGAGGACAGAGCCTTTTAAAACGAGGCGGTGGTG  
CTGCCCTTTAAGGGCGGGCGTCCGGACGACTGTATCTGAGCCCCAGACTGCCCCGA3TTTC  
TGTCGCAGGCTGCGAGGAAAGGCCCTAGGCTGGGTCTGGTGCTTGGCGGCGGCGGCTTCCT  
CCCCGTTGTCNTCCCCGGGCCAGAGGCACCTCGGCTTCAGTCATGCTGAGCAGAGTATGGA  
AGCACCTGACTACGAAGTGCTATCCGTGCGAGAACAGCTATTCCACGAGAGGATCCGCGAGT  
GTATTATATCAACACTTCTGTTTGCAACACTGTACATCNTCTGCCACATCTTCCTGACCCGC  
TTCAAGAAGCCTGCTGAGTTCACCACAGTGGATGATGAAGATGCCACCGTCAACAAGATTGC  
GCTCGAGCTGTGCACCTTTACCCTGGCAATTGCCCTGGGTGCTGTCCTGCTCCTGCCCTTCT  
CCATCATCAGCAATGAGGTGCTGCACTCCC

FIGURE 82

GATGTGCTCCTTGGAGCTGGTGTGCAGTGTCTGACTGTAAGATCAAGTCCAAACCTGTTTT  
GGAATTGAGGAACTTCTCTTTTGATCTCAGCCCTTGGTGGTCCAGGTCTTCATGCTGCTGT  
GGGTGATATTACTGGTCCTGGCTCCTGTCAGTGGACAGTTTGCAAGGACACCCAGGCCCAT  
ATTTTCCTCCAGCCTCCATGGACCACAGTCTTCCAAGGAGAGAGAGTGACCCTCACTTGCAA  
GGGATTTGCTTCTACTCACCACAGAAAACAAAATGGTACCATCGGTACCTTGGGAAAGAAA  
TACTAAGAGAAACCCAGACAATATCCTTGAGGTTTCAGGAATCTGGAGAGTACAGATGCCAG  
GCCCAGGGCTCCCCCTCTCAGTAGCCCTGTGCACTTGGATTTTTCTTCAGAGATGGGATTTCC  
TCATGCTGCCCAGGCTAATGTTGAACTCCTGGGCTCAAGTGATCTGCTCACCTAGGCCTCTC  
AAAGCGCTGGGATTACAGCTTCGCTGATCCTGCAAGCTCCACTTTCTGTGTTTGAAGGAGAC  
TCTGTGGTTCTGAGGTGCCGGGCAAAGGCGGAAGTAACACTGAATAATACTATTTACAAGAA  
TGATAATGTCCTGGCATTCTTAATAAAAGAACTGACTTCCAAAAAAAAAAAAAAAAAAAAA

FIGURE 83

MLLWVILLVLAPVSGQFARTPRP11FLQPPWTTVFQGERVTLTCKGFRFYSPQKTKWYHRYL  
GKEILRETPDNILEVQESGEYRCQAQGSPLSSPVHLD FSSEM GFPHAAQANVELLGSSDLLT

## FIGURE 84

CAGAAGAGGGGGCTAGCTAGCTGTCTCTGCGGACCAGGGAGACCCCCGCGCCCCCGGTGT  
GAGGCGGCCTCACAGGGCCGGGTGGGCTGGCGAGCCGACGCGGCGGCGGAGGAGGCTGTGAG  
GAGTGTGTGGAACAGGACCCGGGACAGAGGAACCAATGGCTCCGCAGAACCTGAGCACCTTTT  
GCCTGTTGCTGCTATACCTCATCGGGGCGGTGATTGCCGGACGAGATTTCTATAAGATCTTG  
GGGGTGCCTCGAAGTGCCCTCTATAAAGGATATTAAAAAGGCCTATAGGAAACTAGCCCTGCA  
GCTTCATCCCGACCGGAACCTGATGATCCACAAGCCCAGGAGAAATTCCAGGATCTGGGTG  
CTGCTTATGAGGTTCTGTCAGATAGTGAGAAACGGAAACAGTACGATACTTATGGTGAAGAA  
GGATTAAAGATGGTCATCAGAGCTCCCATGGAGACATTTTTTTCACACTTCTTTGGGGATTT  
TGGTTTCATGTTTGGAGGAACCCCTCGTCAGCAAGACAGAAATATTCCAAGAGGAAGTGATA  
TTATTGTAGATCTAGAAGTCACTTTGGAAGAAGTATATGCAGGAAATTTTGTGGAAGTAGTT  
AGAAACAAACCTGTGGCAAGGCAGGCTCCTGGCAAACGGAAGTGCAATTGTGCGCAAGAGAT  
GCGGACCACCCAGCTGGGCCCTGGGCGCTTCCAAATGACCCAGGAGGTGGTCTGCGACGAAT  
GCCCTAATGTCAAACCTAGTGAATGAAGAACGAACGCTGGAAGTAGAAATAGAGCCTGGGGTG  
AGAGACGGCATGGAGTACCCCTTTATTGGAGAAGGTGAGCCTCACGTGGATGGGGAGCCTGG  
AGATTTACGGTTCGAATCAAAGTTGTCAAGCACCCAATATTTGAAAGGAGAGGAGATGATT  
TGTACACAAATGTGACAATCTCATTAGTTGAGTCACTGGTTGGCTTTGAGATGGATATTACT  
CACTTGGATGGTCACAAGGTACATATTTCCCGGGATAAGATCACCAGGCCAGGAGCGAAGCT  
ATGGAAGAAAGGGGAAGGGCTCCCCAACTTTGACAACAACAATATCAAGGGCTCTTTGATAA  
TCACTTTTGATGTGGATTTTCCAAAAGAACAGTTAACAGAGGAAGCGAGAGAAGGTATCAAA  
CAGCTACTGAAACAAGGGTCAGTGCAGAAGGTATACAATGGACTGCAAGGATATTGAGAGTG  
AATAAAATTGGACTTTGTTTAAAATAAGTGAATAAGCGATATTTATTATCTGCAAGGTTTTT  
TTGTGTGTGTTTTTGTTTTTATTTTCAATATGCAAGTTAGGCTTAATTTTTTTTATCTAATGA  
TCATCATGAAATGAATAAGAGGGCTTAAGAATTTGTCCATTTGCATTTCGAAAAGAATGACC  
AGCAAAAGGTTTACTAATACCTCTCCCTTTGGGGATTTAATGTCTGGTGCTGCCGCCCTGAGT  
TTCAAGAATTAAAGCTGCAAGAGGACTCCAGGAGCAAAGAAACACAATATAGAGGGTTGGA  
GTTGTTAGCAATTTCAATTCAAAATGCCAACTGGAGAAGTCTGTTTTTAAATACATTTTGTG  
TTATTTTTTA



FIGURE 85

MAPQNLSTFCLLLLYLIGAVIAGRDFYKILGVPRASIKDIKKAYRKLALQLHPDRNPDPPQ  
AQEKFDLGAAYEVLSDSEKQYDQTYGEEGLKDGHQSSHGDISSHFFGDFGFMFGGTTPRQQ  
DRNIPRGSDIIVDLEVTLEEVYAGNFVEVVRNKPVARQAPGKRKCNCRQEMRTTQLGPGRFQ  
MTQEVVCDPCPNVKLVNEERTLEVEIEPGVRDGMETPFGEPEPHVDGEPGDLRFRIKVVKH  
PIFERRGDDLYTNVTISLVESLVGFEMDITHLDGHKVHISRDKITRPGAKLWKKGEGLPNFD  
NNNIKGSIIITFDVDFPKEQLTEEAREGIKQLLKQGSVQKVYNGLQGY

FIGURE 86

TGGGACCAGGGAACCCCGGGCCCCCGGTGGAGNGCCTAACAGGCCGGTGGNTGCGACCGAA  
GCGGCGGGCGGAGGAGGTTTTGAGGATTTTTGGAACAGGACCCGGACAGAGGAACCATGGTT  
CCGCAGAACNTGAGCACNTTTTGCCTGTTGNTGNTATACTTCATCGGGGCGGTGATTGCCGG  
ACGAGATTTNTATAAGATTTTGGGGTGCCTNGAAGTGCCTTNTATAAAGGATATTAAAAAGG  
CCTATAGGAACTAGCCCTGCAGNTTATCCCGACCGGAACCCCTGATGATCCACAAGCCCAG  
GAGAAATTCAGGATTTGGGTGCTGCTTATGAGGTTNTGTGAGATAGTGAGAAACGGAAACA  
GTACGATAATTATGGTGAAGAAGGATTAAAAGATGGTNATCAGAGCTCCCATGGAGACATTT  
TTTCACACTTNTTTGGGGATTTTGGTTTCATGTTTGGAGGAACCCCTNGTCAGCAAGACAGA  
AATATTCCAAGAG

FIGURE 87

GGCACGAGGCGGCGGGGAGTCGCGGGATGCGCCCGGGAGCCACAGCCTGAGGCCCTCAGGT  
CTCTGCAGGTGTCGTGGAGGAACCTAGCACCTGCCATCCTCTTCCCCAATTTGCCACTTCCA  
GCAGCTTTAGCCCATGAGGAGGATGTGACCGGGACTGAGTCAGGAGCCCTCTGGAAGCATGG  
AGACTGTGGTGATTGTTGCCATAGGTGTGCTGGCCACCATCTTTCTGGCTTCGTTTGAGCC  
TTGGTGCTGGTTTGCAGGCAGCGCTACTGCCGCGCGAGACCTGCTGCAGCGCTATGATTC  
TAAGCCCATTGTGGACCTCATTGGTGCCATGGAGACCCAGTCTGAGCCCTCTGAGTTAGAAC  
TGGACGATGTCGTTATCACCAACCCCCACATTGAGGCCATTCTGGAGAATGAAGACTGGATC  
GAAGATGCCTCGGGTCTCATGTCCCACTGCATTGCCATCTTGAAGATTTGTCACTCTGAC  
AGAGAAGCTTGTGGCATGACAATGGGCTCTGGGGCCAAGATGAAGACTTCAGCCAGTGTCA  
GCGACATCATTGTGGTGGCCAAGCGGATCAGCCCCAGGGTGGATGATGTTGTGAAGTCGATG  
TACCCTCCGTTGGACCCCAAACCTCTGGACGCACGGACGACTGCCCTGCTCCTGTCTGTGAC  
TCACCTGGTGCTGGTGACAAGGAATGCCTGCCATCTGACGGGAGGCCTGGACTGGATTGACC  
AGTCTCTGTGCGGCTGCTGAGGAGCATTTGGAAGTCCTTCGAGAAGCAGCCCTAGCTTCTGAG  
CCAGATAAAGGCCTCCAGGCCCTGAAGGCTTCCTGCAGGAGCAGTCTGCAATTTTAGGCCT  
ACAGGCCAGCAGCTAGCCATGAAGGCCCCCTGCCGCCATCCCTGGATGGCTCAGCTTAGCCTT  
CTACTTTTTCTATAGAGTTAGTTGTTCTCCACGGCTGGAGAGTTCAGCTGTGTGTGCATAG  
TAAAGCAGGAGATCCCCGTCAGTTTATGCCTCTTTTGCAGTTGCAAACTGTGGCTGGTGAGT  
GGCAGTCTAATACTACAGTTAGGGGAGATGCCATTCACTCTCTGCAAGAGGAGTATTGAAAA  
CTGGTGGACTGTGAGCTTTATTTAGCTCACCTAGTGTCTTCAAGAAAATTGAGCCACCGTCT  
AAGAAATCAAGAGGTTTACATTAAAATTAGAATTTCTGGCCTCTCTCGATCGGTGAGAATG  
TGTGGCAATTCTGATCTGCATTTTCAGAAGAGGACAATCAATTGAACTAAGTAGGGGTTTC  
TTCTTTTGGCAAGACTTGTACTCTCTCACCTGGCCTGTTTCATTTATTTGTATTATCTGCCT  
GGTCCCTGAGGCGTCTGGGTCTCTCCTCTCCCTTGACAGGTTTGGGTTTGAAGCTGAGGAACT  
ACAAAGTTGATGATTTCTTTTTTATCTTTATGCCTGCAATTTTACCTAGCTACCACTAGGTG  
GATAGTAAATTTATACTTATGTTTCCCTCAAAAAAAAAAAAAA

**FIGURE 88**

METVVIVAIGVLATIFLASFAALVLVCRQRYCRPRDLLQRYDSKPIVDLIGAMETQSEPSEL

~~ELDDVVTITNPHTAILENEDWTEDASGLMSHGTATLKTCHTLTEKLVAMTMGSCAKMKTSAS~~

VSDIIVVAKRISPRVDDVVKSMYPPLDPKLLDARTTALLSVSHLVLVTRNACHLTGGLDWI

DQSLSAEEHLEVLREAALASEPDKGLPGPEGFLQEQSAI

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FIGURE 89

GCTTCATTTCTCCCGACTCAGCTTCCCACCCTGGGCTTCCGAGGTGCTTTCGCCGCTGTCC  
CCACCACTGCAGCCATGATCTCCTTAACGGACACGCAGAAAATTGGAATGGGATTAACAGGA  
TTTGGAGTGTTTTCTGTCTTTGGAATGATTCTCTTTTTTGACAAAGCACTACTGGCTAT  
TGGAAATGTTTTATTTGTAGCCGGCTTGGCTTTTGTAATTGGTTTAGAAAGAACATTCAGAT  
TCTTCTTCCAAAAACATAAAATGAAAGCTACAGGTTTTTTTTCTGGGTGGTGTATTTGTAGTC  
CTTATTGGTTGGCCTTTGATAGGCATGATCTTCGAAATTTATGGATTTTTCTCTGTTCAG  
GGGCTTCTTCCGTGTCGTTGTTGGCTTTATTAGAAGAGTGCCAGTCCTTGGATCCCTCCTAAAT  
TTACCTGGAATTAGATCATTTGTAGATAAAGTTGGAGAAAGCAACAATATGGTATTAACAACA  
AGTGAATTTGAAGACTCATTTAAAATATTGTGTTATTTATAAAGTCATTTGAAGAATATTCA  
GCACAAAATTAAATTACATGAAATAGCTTGTAATGTTCTTTACAGGAGTTTAAAACGTATAG  
CCTACAAAGTACCAGCAGCAAATTAGCAAAGAAGCAGTGAAAACAGGCTTCTACTCAAGTGA  
ACTAAGAAGAAGTCAGCAAGCAAAGTGAAGAGAGGTGAAATCCATGTTAATGATGCTTAAGAA  
ACTCTTGAAGGCTATTTGTGTTGTTTTCCACAATGTGCGAAACTCAGCCATCCTTAGAGAA  
CTGTGGTGCCTGTTTCTTTCTTTTTATTTTGAAGGCTCAGGAGCATCCATAGGCATTTGCT  
TTTTAGAAGTGTCCACTGCAATGGCAAAAATATTTCCAGTTGCACTGTATCTCTGGAAGTGA  
TGCATGAATTCGATTGGATTGTGTCATTTTAAAGTATTAAAACCAAGGAAACCCCAATTTTG  
ATGTATGGATTACTTTTTTTTTGNGCNCAGGGCC

## **FIGURE 90**

MISLTDQTQKIGMGLTGFGVFFLFFGMILFFDKALLAIGNVLFVAGLAFVIGLERTFRFFFQK  
HKMKATGFFLGGVFVVLIGWPLIGMIFEIYGFFLLFRGFFPVVVGFIIRVPVLGSLLNLPGI  
RSFVDKVGESNNMV

**Important features:**

**Transmembrane domains:**

amino acids 12-30 (typeII), 33-52, 69-89 and 93-109

**N-myristoylation sites.**

amino acids 11-16, 51-56 and 116-121

**Aminoacyl-transfer RNA synthetases class-II protein.**

amino acids 49-59

FIGURE 91

GAAGACGTGGCGGCTCTCGCCTGGGCTGTTTCCCGGCTTCATTTCTCCCGACTCAGCTTCCC  
ACCNTGGGCTTTCCGAGGTGCTTTGCGCCGCTGTCCCCA<sup>~</sup>CCACTGCAGCCATGATCTCCTTAA  
CGGACACGCAGAAAAATTGGAATGGGATTAACCGGATTTGGAGTGTTTTTCTGTCTTTTGA  
ATGATTCTCTTTTTTGACAAAGCACTACTGGCTATTGGAAATGTTTTATTTGTAGCCGGCTT  
GGCTTTTGTAAATTGGTTTAGAAAGAACATTCAGATTCTTCTTCCAAAAACATAAAATGAAAG  
CTACAGGTTTTTTTTCTGGGTGGTGTATTTGTAGTCCTTATTGGTTGGCCTTTGATAGGCATG  
ATCTTCGAAATTTATGGATTTTTTCTCTTGTTT

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FIGURE 92

GGCACGAGGCTGAACCCAGCCGGCTCCATCTCAGCTTCTGGTTTCTAAGTCCATGTGCCAAA  
GGCTGCCAGGAAGGAGACGCCTTCCTGAGTCCTGGATCTTTCTTCCTTCTGGAAATCTTTGA  
CTGTGGGTAGTTATTTATTTCTGAATAAGAGCGTCCACGCATCATGGACCTCGCGGGACTGC  
TGAAGTCTCAGTTCCTGTGCCACCTGGTCTTCTGCTACGTCTTTATTGCCTCAGGGCTAATC  
ATCAACACCATTTCAGCTCTTCACTCTCCTCCTCTGGCCCATTAACAAGCAGCTCTTCCGGAA  
GATCAACTGCAGACTGTCCTATTGCATCTCAAGCCAGCTGGTGATGCTGCTGGAGTGGTGGT  
CGGGCACGGAATGCACCATCTTCACGGACCCGCGCGCTACCTCAAGTATGGGAAGGAAAAT  
GCCATCGTGGTTCTCAACCACAAGTTTGAAATTGACTTTCTGTGTGGCTGGAGCCTGTCCGA  
ACGCTTTGGGCTGTTAGGGGGCTCCAAGGTCTGGCCAAGAAAGAGCTGGCCTATGTCCCAA  
TTATCGGCTGGATGTGGTACTTCACCGAGATGGTCTTCTGTTCGCGCAAGTGGGAGCAGGAT  
CGCAAGACGGTTGCCACCAGTTTGCAGCACCTCCGGGACTACCCCGAGAAGTATTTTTTCT  
GATTCACTGTGAGGGCACACGGTTCACGGAGAAGAAGCATGAGATCAGCATGCAGGTGGCCC  
GGGCAAGGGGCTGCCTCGCCTCAAGCATCACCTGTTGCCACGAACCAAGGGCTTCGCCATC  
ACCGTGAGGAGCTTGAGAAATGTAGTTTTCAGCTGTATATGACTGTACACTCAATTTAGAAA  
TAATGAAAATCCAACACTGCTGGGAGTCCTAAACGGAAAGAAATACCATGCAGATTTGTATG  
TTAGGAGGATCCCACTGGAAGACATCCCTGAAGACGATGACGAGTGCTCGGCCTGGCTGCAC  
AAGCTCTACCAGGAGAAGGATGCCTTTTCAGGAGGAGTACTACAGGACGGGCACCTTCCCAGA  
GACGCCCATGGTGCCCCCGCGGCCCTGGACCCTCGTGAAGTGGCTGTTTTGGGCCTCGC  
TGGTGCTCTACCCTTCTTCCAGTTCCTGGTCAGCATGATCAGGAGCGGGTCTTCCCTGACG  
CTGGCCAGCTTCATCCTCGTCTTCTTTGTGGCCTCCGTGGGAGTTCGATGGATGATTGGTGT  
GACGGAAATTGACAAGGGCTCTGCCTACGGCAACTCTGACAGCAAGCAGAACTGAATGACT  
GACTCAGGGAGGTGTCACCATCCGAAGGGAACCTTGGGGAACTGGTGGCCTCTGCATATCCT  
CCTTAGTGGGACACGGTGACAAAGGCTGGGTGAGCCCCCTGCTGGGCACGGCGGAAGTCACGA  
CCTCTCCAGCCAGGAGTCTGGTCTCAAGGCCGATGGGGAGGAAGATGTTTTGTAATCTTT  
TTTTCCCCATGTGCTTTAGTGGGCTTTGGTTTTCTTTTTGTGCGAGTGTGTGTGAGAATGGC  
TGTGTGGTGAGTGTGAACTTTGTCTGTGATCATAGAAAGGTATTTTAGGCTGCAGGGGAG  
GGCAGGGCTGGGGACCGAAGGGGACAAGTTCCCTTTTCATCCTTTGGTGCTGAGTTTCTGT  
AACCCTTGGTTGCCAGAGATAAAGTGAAAAGTGCTTTAGGTGAGATGACTAAATTATGCCTC  
CAAGAAAAAAAAAATTAAAGTGCTTTTCTGGGTCAAAAAAAAAA



FIGURE 93

MDLAGLLKSQFLCHLVFCYVFIA SGLIINTIQLF TLLLWPINKQLFRKINCRLSYCISSQLV  
MLEWWSGTECTIFTDPRAYLKYGKENAIVVLN HKFEIDFLCGWSLSERFGLLGGSKVLAKK  
ELAYVPIIGWMWYFTEMVFCSRKWEQDRKTVATSLQH LRDYPEKYFFLIHCEGTRFTEKKHE  
ISMQVARAKGLPRLKHLLPRTKGFAITVRS LRNVVSAVYDCTLNFRNNENPTLLGV LNKKK  
YHADLYVRRIPLEDIPEDDDECSAWLHKLYQEKDAFQEEYYRTGTFPETPMVPPRRPWT LVN  
WLFWASLVLYPFFQFLVSMIRSGSSLTLASFILVFFVASVGVRWMIGVTEIDKGSAYGNSDS  
KQKLND

FIGURE 94

CTGAGGCGGCGGTAGCATGAGGGGGAGAGTACGTCGGCGGTGCTCTCGGGCTTTGTGCTCG  
GCGCACTCGCTTTCCAGCACCTCAACACGGACTCGGACACGGAAGGTTTTCTTCTTGGGGAA  
GTAAAAGGTGAAGCCAAGAACAGCATTACTGATTCCCAAATGGATGATGTTGAAGTTGTTTA  
TACAATTGACATTAGAAATATATTCCATGCTATCAGCTTTTGTAGCTTTTATAATTCTTCAG  
GCGAAGTAAATGAGCAAGCACTGAAGAAAATATTATCAAATGTCAAAAAGAATGTGGTAGGT  
TGGTACAAATCCGTCGTCAATCAGATCAGATCATGACGTTTAGAGAGAGGCTGCTTCACAA  
AACTTGCAGGAGCATTTTTCAAACCAAGACCTTGTTTTCTGCTATTAACACCAAGTATAA  
TAACAGAAAAGCTGCTCTACTCATCGACTGGAACATTCCTTATATAAACCTCAAAAAGGACTT  
TTTCACAGGGTACCTTTAGTGGTTGCCAATCTGGGCATGTCTGAACAACTGGGTATATAAAC  
TGTATCAGGTTCCGTGTATGTCCACTGGTTTTAGCCGAGCAGTACAAACACACAGCTCTAAAT  
TTTTTGAAGAAGATGGATCCTTAAAGGAGGTACATAAGATAAATGAAATGTATGCTTCATTA  
CAAGAGGAATTAAAGAGTATATGCAAAAAAGTGGAAGACAGTGAACAAGCAGTAGATAAACT  
AGTAAAGGATGTAAACAGATTAAACGAGAAATTGAGAAAAGGAGAGGAGCACAGATTCAGG  
CAGCAAGAGAGAAGAACATCCAAAAAGACCTCAGGAGAACATTTTTCTTTGTGTCAGGCATTA  
CGGACCTTTTTTCCAAATTCTGAATTTCTTCATTATGTGTTATGTCTTTAAAAAATAGACA  
TGTTTCTAAAAGTAGCTGTAACCTACAACCACCATCTCGATGTAGTAGACAATCTGACCTTAA  
TGGTAGAACACACTGACATTCCTGAAGCTAGTCCAGCTAGTACACCACAAATCATTAAAGCAT  
AAAGCCTTAGACTTAGATGACAGATGGCAATTCAAGAGATCTCGGTTGTTAGATACACAAGA  
CAAACGATCTAAAGCAAATACTGGTAGTAGTAACCAAGATAAAGCATCCAAAAATGAGCAGCC  
CAGAAACAGATGAAGAAATTGAAAAGATGAAGGGTTTTGGTGAATATTCACGGTCTCCTACA  
TTTTGATCCTTTTAACCTTACAAGGAGATTTTTTTATTTGGCTGATGGGTAAAGCCAAACAT  
TTCTATTGTTTTTACTATGTTGAGCTACTTGCAGTAAGTTCATTTGTTTTTACTATGTTTAC  
CTGTTTGCAGTAATACACAGATAACTCTTAGTGCATTTACTTCACAAAGTACTTTTTTCAAAC  
ATCAGATGCTTTTATTTCCAAACCTTTTTTTCACCTTTCACTAAGTTGTTGAGGGGAAGGCT  
TACACAGACACATTCCTTAGAATTGGAAAAAGTGAGACCAGGCACAGTGGCTCACACCTGTAA  
TCCCAGCACTTAGGGAAGACAAGTCAGGAGGATTGATTGAAGCTAGGAGTTAGAGACCAGCC  
TGGGCAACGTATTGAGACCATGTCTATTAATAAATAAATGAAAAAGCAAGAATAGCCTTAT  
TTTCAAAATATGGAAGAAATTTATATGAAATTTATCTGAGTCATTAAAATTCTCCTTAAG  
TGATACTTTTTTAGAAGTACATTATGGCTAGAGTTGCCAGATAAAATGCTGGATATCATGCA  
ATAAATTTGCAAAACATCATCTAAAAATTTAAAAAAAAAAAAAAAAAAAAAAAAA

FIGURE 95

MEGESTSAVLSGFVLGALAFQHLNTSDTEGFLLEVKGEAKNSITDSQMDDVEVVYTTIDIQ  
KYIPCYQLFSFYNSSGEVNEQALKKILSNVKKNVVGWYKFRRHSDQIMTFRERLLHKNLQEH  
FSNQDLVFLLLTPSIITESCSTHRLEHSLYKPQKGLFHRVPLVVANLGMSEQLGYKTVSGSC  
MSTGFSRAVQTHSSKFFEEEDGSLKEVHKINEMYASLQEELKSICKKVEDSEQAVDKLVKDVN  
RLKREIEKRRGAQIQAAREKNIQKDPQENIFLCQALRTFFPNSEFLHSCVMSLKNRHVSKSS  
CNYNHLDVVDNLTLMVEHTDIPEASPASTPQIIKHKALDLDLDRWQFKRSRLDLDQDKRSKA  
NTGSSNQDKASKMSSPETDEEIEKMKGFGEYSRSPTF

FIGURE 96

GGCACAGCCGCGCGGCGGAGGGCAGAGTCAGCCGAGCCGAGTCCAGCCGGACGAGCGGACCA  
GCGCAGGGCAGCCCAAGCAGCGCGCAGCGAACGCCCGCCGCGCCACACCCTCTGCGGTCC  
CCGCGGCGCCTGCCACCCTTCCCTCCTTCCCCGCGTCCCCGCTCGCCGGCCAGTCAGCTTG  
CCGGGTTGCTGCCCCGCGAAACCCGAGGTACCAGCCCGCGCCTCTGCTTCCCTGGGCCG  
CGCGCCGCTCCACGCCCTCCTTCTCCCCGCGTCTCCTCCGCTGCTCGCCTCTTCCACCA  
GACGCGAGGCCAGCTCTACTTTTCCCCCGCGTCTCCTCCGCTGCTCGCCTCTTCCACCA  
ACTCCAACCTCCTTCTCCCTCCAGCTCCACTCGCTAGTCCCCGACTCCGCCAGCCCTCGGCC  
GCTGCCGTAGCGCCGCTTCCCGTCCGGTCCCAAAGGTGGGAACGCGTCCGCCCCGGCCCCGA  
CCATGCGACGGTTGCGCTTGCCCCGCGCTTCTCTGCACCCCTGGCAGTGCTCAGCGCCGCGCTG  
CTGGCTGCCGAGCTCAAGTCGAAAAGTTGCTCGGAAGTGCGACGCTCTTACGTGTCCAAAGG  
CTTCAACAAGAACGATGCCCCCTCCACGAGATCAACGGTGATCATTGAGATCTGTCCCC  
AGGGTTCTACCTGCTGCTCTCAAGAGATGGAGGAGAAGTACAGCCTGCAAGTAAAGATGAT  
TTCAAAAGTGTTGGTCAGCGAACAGTGCAATCATTTGCAAGCTGTCTTTGCTTACGTTACAA  
GAAGTTTGATGAATTTCTTCAAAGAACTACTTGAAAATGCAGAGAAATCCCTGAATGATATGT  
TTGTGAAGACATATGGCCATTTATACATGCAAAATTTCTGAGCTATTTAAAGATCTCTTCGTA  
GAGTTGAAACGTTACTACGTGGTGGGAAATGTGAACCTGGAAGAAATGCTAAATGACTTCTG  
GGCTCGCCTCCTGGAGCGGATGTTCCGCTGGTGAACTCCAGTACCACTTTACAGATGAGT  
ATCTGGAATGTGTGAGCAAGTATACGGAGCAGCTGAAGCCCTTCGGAGATGTCCCTCGCAA  
TTGAAGCTCCAGGTTACTCGTGCTTTTGTAGCAGCCCGTACTTTCTGCTCAAGGCTTAGCGGT  
TGCGGGAGATGTGCTGAGCAAGGTCTCCGTGGTAAACCCACAGCCAGTGATCCCATGCCC  
TGTTGAAGATGATCTACTGCTCCCACTGCCGGGGTCTCGTGACTGTGAAGCCATGTTACAAC  
TACTGCTCAAACATCATGAGAGGCTGTTTGGCCAACCAAGGGGATCTCGATTTTGAATGGAA  
CAATTTCATAGATGCTATGCTGATGGTGGCAGAGAGGCTAGAGGGTCCTTTCAACATTGAAT  
CGGTCATGGATCCCATCGATGTGAAGATTTCTGATGCTATTATGAACATGCAGGATAATAGT  
GTTCAAGTGTCTCAGAAGGTTTTCCAGGGATGTGGACCCCCCAAGCCCTCCAGCTGGACG  
AATTTCTCGTTCCATCTCTGAAAGTGCCCTCAGTGCTCGCTTCAGACCACATCACCCGAGG  
AACGCCCCAACCAAGCAGCTGGCACTAGTTTGGACCGACTGGTTACTGATGTCAAGGAGAAA  
CTGAAACAGGCCAAGAAATTTCTGGTCCCTCCCTTCCGAGCAACGTTTGCAACGATGAGAGGAT  
GGCTGCAGGAAACGGCAATGAGGATGACTGTTGGAATGGGAAAGGCAAAAGCAGGTACCTGT  
TTGCAGTGACAGGAAATGGATTAGCCAACCAAGGGCAACAACCCAGAGGTCCAGGTTGACACC  
AGCAAACAGACATACTGATCCTTCGTCAAATCATGGCTCTTCGAGTGATGACCAGCAAGAT  
GAAGAATGCATACAATGGGAACGACGTGGACTTCTTTGATATCAGTGATGAAAGTAGTGGAG  
AAGGAAGTGGAAGTGGCTGTGAGTATCAGCAGTGCCCTTCAGAGTTTGACTACAAATGCCACT  
GACCATGCTGGGAAGAGTGCCAAATGAGAAAGCCGACAGTGCTGGTGTCCGTCTCGGGGCACA  
GGCCTACCTCCTCACTGTCTTCTGCATCTTGTTCCTGGTTATGCAGAGAGAGTGGAGATAAT  
TCTCAAACCTCTGAGAAAAAGTGTTCATCAAAAAGTTAAAAGGCACCAAGTTATCACTTTTCTA  
CCATCCTAGTGACTTTGCTTTTAAATGAATGGACAACAATGTACAGTTTTTACTATGTGGC  
CACTGGTTTAAAGAAGTGCTGACTTTGTTTTCTCATTAGTTTTTGGAGGAAAAGGGACTGTG  
CATTGAGTTGGTTCTGCTCCCCCAAACCATGTTAAACGTGGCTAACAGTGATAGGTACAGAA  
CTATAGTTAGTTGTGCATTTGTGATTTTATCACTCTATTATTTGTTTGTATGTTTTTTTCTC  
ATTTCTGTTTGTGGGTTTTTTTTTCCAACGTGTGATCTCGCCTTGTCTTTTACAAGCAAACAG  
GGTCCCTTCTTGGCACGTAACATGTACGTATTTCTGAAATATTAAATAGCTGTACAGAAGCA  
GGTTTTATTTATCATGTTATCTTATTAAAAAGAAAAAGCCCAAAAGC

FIGURE 97

MARFGLPALLCTLAVLSAALLAELKSKSCSEVRRLYVSKGFNKNDAPLHEINGDHLKICPQ  
GSTCCSQEMEEKYSLQSKDDFKSVVSEQCNHLQAVFASRYKKFDEFKELLENAEKSLNDMF  
VKTYGHLYMQNSELFKDLFVELKRYVVGNNLEMLNDFWARLLERMFRLVNSQYHFTDEY  
LECVSKYTEQLKPFQDVPRKLLQVTRAFVAARTFAQGLAVAGDVVSKVSVVNPTAQCTHAL  
LKMIYCSHCRGLVTVKPCYNYCSNIMRGCLANQGDLD FEWNNFIDAMLMVAERLEGPFNIES  
VMDPIDVKISDAIMNMQDNSVQVSQKVFQGC GPPKPLPAGRISRSISESAFSARFRPHHPEE  
RPTTAAGTSLDRLVTDVKEKLQAKKFWSSLPSNVCNDERMAAGNGNEDDCWNGKGKSRYL  
AVTGNGLANQGNNPEVQVDTSKPDILILRQIMALRVMTSKMKNAYNGNDVDFFDISDESSGE  
GSGSGCEYQQCPSEFDYNATDHAGKSANEKADSAGVRPGAQAYLLTVFCILFLVMQREWR

FIGURE 98

CTCGCCCTCAAATGGGAACGCTGGCCTGGGACTAAAGCATAGACCACCAGGCTGAGTATCCT  
GACCTGAGTCATCCCCAGGGATCAGGAGCCTCCAGCAGGGAACCTTCCATTATATTCTTCAA  
GCAACTTACAGCTGCACCGACAGTTGCGATGAAAGTTCTAATCTCTTCCCTCCTCCTGTTGC  
TGCCACTAATGCTGATGTCCATGGTCTCTAGCAGCCTGAATCCAGGGGTCGCCAGAGGCCAC  
AGGGACCGAGGCCAGGCTTCTAGGAGATGGCTCCAGGAAGGCGGCCAAGAATGTGAGTGCAA  
AGATTGGTTCCTGAGAGCCCCGAGAAGAAAATTTCATGACAGTGTCTGGGCTGCCAAAGAAGC  
AGTGCCCCCTGTGATCATTTCAAGGGCAATGTGAAGAAAACAAGACACCAAAGGCACCACAGA  
AAGCCAAACAAGCATTCCAGAGCCTGCCAGCAATTTCTCAAACAATGTCAGCTAAGAAGCTT  
TGCTCTGCCTTTGTAGGAGCTCTGAGCGCCCACTCTTCCAATTAAACATTCTCAGCCAAGAA  
GACAGTGAGCACACCTACCAGACACTCTTCTTCTCCACCTCACTCTCCCACTGTACCCACC  
CCTAAATCATTCCAGTGCTCTCAAAAAGCATGTTTTTCAAGATCATTTTGTGTTGCTCTC  
TCTAGTGTCTTCTTCTCTCGTCAGTCTTAGCCTGTGCCCTCCCCTTACCCAGGCTTAGGCTT  
AATTACCTGAAAGATTCCAGGAACTGTAGCTTCCTAGCTAGTGTCAATTAACCTTAAATGC  
AATCAGGAAAGTAGCAAACAGAAGTCAATAAATATTTTTAAATGTCAAAAAAAAAAAAAAAAAA

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**FIGURE 99**

MKVLISLLLLLPLMLMSMVSSSLNPGVARGHRDRGQASRRWLQEGGQECECKDWFLRAPRR  
KFMTVSGLPKKQCPCDHFKGNVKKTRHQRHHRKPNKHSRACQQFLKQCQLRSFALPL

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FIGURE 100

AATGGCTGTCTTAGTACTTCGCCTGACAGTTGTCCTGGGACTGCTTGTCTTATTCTTGACCT  
GCTATGCAGACGACAAACCAAGACAAGCCAGACGACAAGCCAGACGACTCGGGCAAAGACCCA  
AAGCCAGACTTCCCCAAATTCCTAAGCCTCCTGGGCACAGAGATCATTGAGAATGCAGTCGA  
GTTTCATCCTCCGCTCCATGTCCAGGAGCACAGGATTTATGGAATTTGATGATAATGAAGGAA  
AACATTTCATCAAAGTGAATCCTCAGGACACACCCATGTGGCTCCTGGACAATCCAAGAGCA  
GCCAAATCCTGCTTTTCCAGTTTGGCTCCACAAGTCCTCCAGGACAGAGCCCTCAAAGCAAC  
TCCCAACGAGTTCTCAGGATTCAGGCTCTGGCTTCAACCAAACAGAACTCATTTTGAACACC  
CTGACTGCATTTTTGCTTTTAGAAAGTTAGAATAAATATGGCGCTTTGGGATCACATAGTTG  
ATGGAGAGGAAA



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FIGURE 101

MAVLVLRLTVVLGLLVLFLTCYADDKPKDPDDKPDGKDPKPDFPKFLSLLGTEI IENAVE  
FILRSMRSTGFMEFDDNEGKHSSK

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FIGURE 102

GGACGCCAGCGCCTGCAGAGGCTGAGCAGGGAAAAAGCCAGTGCCCCAGCGGAAGCACAGCT  
CAGAGCTGGTCTGCCATGGACATCCTGGTCCCCTCCTGCAGCTGCTGGTGCTGCTTCTTAC  
CCTGCCCCCTGCACCTCATGGCTCTGCTGGGCTGCTGGCAGCCCCCTGTGCAAAAGCTACTTCC  
CCTACCTGATGGCCGTGCTGACTCCCAAGAGCAACCGCAAGATGGAGAGCAAGAAACGGGAG  
CTCTTCAGCCAGATAAAAGGGGCTTACAGGAGCCTCCGGGAAAGTGGCCCTACTGGAGCTGGG  
CTGCGGAACCGGAGCCAACTTTAGTTCTACCCACCGGGCTGCAGGGTCACCTGCCTAGACC  
CAAAATCCCCACTTTGAGAAGTTCCTGACAAAGAGCATGGCTGAGAACAGGCACCTCCAATAT  
GAGCGGTTTGTGGTGGCTCCTGGAGAGGACATGAGACAGCTGGCTGATGGCTCCATGGATGT  
GGTGGTCTGCACTCTGGTGCTGTGCTCTGTGCAGAGCCCAAGGAAGGTCCTGCAGGAGGTCC  
GGAGAGTACTGAGACCGGGAGGTGTGCTCTTTTTCTGGGAGCATGTGGCAGAACCATATGGA  
AGCTGGGCCTTCATGTGGCAGCAAGTTTTGAGCCCACTTGAAACACATTGGGGATGGCTG  
CTGCCTCACCAGAGAGACCTGGAAGGATCTTGAGAACGCCCAGTTCTCCGAAATCCAAATGG  
AACGACAGCCCCCTCCCTTGAAGTGGCTACCTGTTGGGCCCCACATCATGGGAAAGGCTGTC  
AAACAATCTTTCCCAAGCTCCAAGGCACTCATTTGCTCCTTCCCCAGCCTCCAATTAGAACA  
AGCCACCCACCAGCCTATCTATCTTCCACTGAGAGGGACCTAGCAGAATGAGAGAAGACATT  
CATGTACCACCTACTAGTCCCTCTCTCCCCAACCTCTGCCAGGGCAATCTCTAACTTCAATC  
CCGCCTTCGACAGTGAAAAAGCTCTACTTCTACGCTGACCCAGGGAGGAAACACTAGGACCC  
TGTTGTATCCTCAACTGCAAGTTTCTGGACTAGTCTCCCAACGTTTGCCTCCCAATGTTGTC  
CCTTTCCTTCGTTCCCATGGTAAAGCTCCTCTCGCTTTCCTCCTGAGGCTACACCCATGCGT  
CTCTAGGAACGGTCAAAAAGTCATGGTGCCTGCATCCCTGCCAAGCCCCCTGACCCCTCT  
CTCCCCACTACCACCTTCTTCTGAGCTGGGGGCACCAGGGAGAATCAGAGATGCTGGGGAT  
GCCAGAGCAAGACTCAAAGAGGCAGAGGTTTTGTTCTCAAATATTTTTTAATAAATAGACGA  
AACCACG

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FIGURE 103

MDILVPLLQLLVLLLTLPPLHLMALLGCWQPLCKSYFPYLMAVLTPKSNRKMESKKRELFSQL  
KGLTGASGKVALLELGCGTGANFQFYPPGCRVTCCLDPNPHFEKFLTKSMAENRHLQYERFVV  
APGEDMRQLADGSMDVVVCTLVLCVQSPRKVLQEVRRVLRPGGVLEFFWEHVAEPYGSWAFM  
WQQVFEPTWKHIGDGCCLTRETWKDLENAQFSEIQMERQPPPLKWLPGPHIMGKAVKQSF  
SSKALICSFPSLQLEQATHQPIYLPLRGT

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FIGURE 104

GTGGGATTTATTTGAGTGCAAGATCGTTTTCTCAGTGGTGGTGGAAAGTTGCCTCATCGCAGG  
CAGATGTTGGGGCTTTGTCCGAACAGCTCCCCCTCTGCCAGCTTCTGTAGATAAGGGTTAAA  
ACTAATATTTATATGACAGAAGAAAAAGATGTCATTCCGTAAAGTAAACATCATCATCTTGG  
TCCTGGCTGTTGCTCTCTTCTTACTGGTTTTGCACCATAACTTCCTCAGCTTGAGCAGTTTG  
TTAAGGAATGAGGTTACAGATTGAGGAATTGTAGGGCCTCAACCTATAGACTTTGTCCCAA  
TGCTCTCCGACATGCAGTAGATGGGAGACAAGAGGAGATTCTGTGGTCATCGCTGCATCTG  
AAGACAGGCTTGGGGGGGCCATTGCAGCTATAAACAGCATTGAGCACAACACTCGCTCCAAT  
GTGATTTTCTACATTGTTACTCTCAACAATACAGCAGACCATCTCCGGTCTGGCTCAACAG  
TGATTCCCTGAAAAGCATCAGATACAAAATTGTCAATTTTGACCCTAAACTTTTGGAAGGAA  
AAGTAAAGGAGGATCCTGACCAGGGGAATCCATGAAACCTTTAACCTTTGCAAGGTTCTAC  
TTGCCAATTCTGGTTCCCAGCGCAAAGAAGGCCATATACATGGATGATGATGTAATTGTGCA  
AGGTGATATTCTTGCCCTTTACAATACAGCACTGAAGCCAGGACATGCAGCTGCATTTTCAG  
AAGATTGTGATTGAGCCTCTACTAAAGTTGTCATCCGTGGAGCAGGAAACCAGTACAATTAC  
ATTGGCTATCTTGACTATAAAAAGGAAAGAATTTCGTAAGCTTTCCATGAAAGCCAGCACTTG  
CTCATTTAATCCTGGAGTTTTTTGTTGCAAACCTGACGGAATGGAAACGACAGAATATAACTA  
ACCAACTGGAAAAATGGATGAAACTCAATGTAGAAGAGGGACTGTATAGCAGAACCTGGCT  
GGTAGCATCACAACACCTCCTCTGCTTATCGTATTTTATCAACAGCACTCTACCATCGATCC  
TATGTGGAATGTCCGCCACCTTGGTTCCAGTGCTGGAAAACGATATTCACCTCAGTTTGTA  
AGGCTGCCAAGTTACTCCATTGGAATGGACATTTGAAGCCATGGGGAAGGACTGCTTCATAT  
ACTGATGTTTGGGAAAAATGGTATATTCCAGACCCAACAGGCAAATTC AACCTAATCCGAAG  
ATATACCGAGATCTCAAACATAAAGTGAAACAGAATTTGAACTGTAAGCAAGCATTCTCAG  
GAAGTCCTGGAAGATAGCATGCATGGGAAGTAACAGTTGCTAGGCTTCAATGCCTATCGGTA  
GCAAGCCATGGAAAAAGATGTGTGCTAGGTAAAGATGACAACTGCCCTGTCTGGCAGTC  
AGCTTCCCAGACAGACTATAGACTATAAATATGTCTCCATCTGCCTTACCAAGTGTCTTCTT  
ACTACAATGCTGAATGACTGGAAAGAAGAACTGATATGGCTAGTTCAGCTAGCTGGTACAGA  
TAATTCAAAACTGCTGTTGGTTTTAATTTTGTAACCTGTGGCCTGATCTGTAAATAAACTT  
ACATTTTTC

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FIGURE 105

MSFRKVNIIILVLAVALFLLVLHHNFLSLSSLRNEVTDSGIVGPQPIDFVPNALRHAVDGR  
QEEIPVVIAASEQRLGGAIAAINS IQHNTRSNVIFYIVTLNNTADHLRSWLNSDSLKSIRYK  
IVNFDPKLLEGKVKEDPDQGESMKPLTFARFYLPILVPSAKKAIYMDDDVIVQGDILALYNT  
ALKPGHAAAFSEDCDSASTKV VIRGAGNQNYIGYLDYKKERIRKLSMKASTCSFNPGVFVA  
NLTEWKRQNI TNQLEKWMKLNVEEGLYSRTL AGSITTPPLLIVFYQQHSTIDPMWNVRLGS  
SAGKRYSPQFVKAALLHWNGHLKPWGRTASYTDVWEKWYIPDPTGKFNLIRRYTEISNIK

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FIGURE 106

TGGTTTTTGCCCCATAAATTCCTCAGCTTGAGCAGTTTGTTAAGGAATGAGGTTACAGATT  
CAGGAATTNTAGGNCCTCAACCTNTAGANTTTGTCCCAAATGTTCTCCGACATGCAGTAGAT  
GGGAGACAAGAGGAGATTCTGTGGTCATCGCTGCATNTGAAGACAGGCTTGGGGGGGCCAT  
TGCAGCTATAAACAGCATTTCAGCACAACTCGNTCCAATGTGATTTTCTACATTGTTACTC  
TCAACAATACAGCAGACCATNTCCGGTCTTGGNTCAACAGTGATTCCCTGAAAAGCATCAGA  
TACAAAATTGTCAATTTTGACCCCTAACTTTTGGAAGGAAAAGTAAAGGAGGATCCTGACCA  
GGGGGAATCCATGAAACCTTTAACCTTTGCAAGGTTCTACTTGCCAATTCTGGTTCCCAGCG  
CAAAGAAGGCCATATACATGGATGATGATGTAATTGTGCAAGGTGATATTCTTGCCCTTTAC  
AATACAGCACTGAAGCCAGGACATGCAGCTGCATTTTCAGAAGATTGTGATTCAGCCTCTAC  
TAAAGTTGTCATCCGTGGAGCAGGAAA

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FIGURE 107

CGACGCTCTAGCGGTTACCGCTGCGGGCTGGCTGGGCGTAGTGGGGCTGCGCGGCTGCCACG  
GAGCTAGAGGGCAAGTGTGCTCGGCCCAGCGTSCAGGGAACGCGGGCGGCCAGACAACGGGC  
TGGGCTCCGGGGCCTGCGGCGCGGGCGCTGAGCTGGCAGGGCGGGTCCGGGCGCGGGCTGCA  
TCCGCATCTCCTCCATCGCCTGCAGTAAGGGCGGCCGCGGCGAGCCTTTGAGGGGAACGACT  
TGTCGGAGCCCTAACCAGGGGTGTCTCTGAGCCTGGTGGGATCCCCGAGCGTCACATCACT  
TTCCGATCACTTCAAAGTGGTTAAAACTAATATTTATATGACAGAAGAAAAAGATGTCATT  
CCGTAAAGTAAACATCATCATCTTGGTCCTGGGCTGTTGCTCTCTTCTTACTGGTTTTGCAC  
CATAACTTCCTCAGCTTGAGGCAGTTTGTTAAGGAATGAGGTTACAGATTGAGGAATTGTAG  
GGCCTCAACCTATAGGACTTTGTCCCAAATGCTCTCCGACATGCAGTAGATGGGAGACAAGA  
GGAGATTCTGTGGTCATCGCTGCATCTGAAGACAGGCTTGGGGGGGCCATTGCAGCTATAA  
ACAGCATTGAGCACAACACTCGCTCCAATGTGATTTTCTACATTGTTACTCTCAACAATACA  
GCAGACCATCTCCGGTCCTGGGCTCAACAGTGATTCCCTGAAAAGCATCAGATACAAAATTG  
TCAATTTTGACCCTAACTTTTGAAGGAAAAGTAAAGGAGGATCCTGACCAGGGGGAATCC  
ATGAAACCTTTAACCTTTGCAAGGTTCTACTTGCCAATTCTGGGTTCCAGCGCAAAGAAGG  
CCATATACATGGATGATGATGTAATTGTGCAAGGTGATATTCTTGCCCTTTACAATACAGCA  
CTGAAGCCAGGACATGCAGCTGCATTTTCAGAAGATTGTGATTGAGCCTCTACTAAAGTTGT  
CATCCGTGGAGCAGGAAACCAGTACAATTACATTGGCTATCTTGACTATAAAAAGGAAAGAA  
TTCGTAAGCTTTCCATGAAAGCCAGCACTTGCTCATTTAATCCTGGAGTTTTTGTGTGCAAC  
CTGACGGAATGGAAACGACAGAATATACTAACCAACTGGAAAAATGGATGAAACTCAATGT  
AGAAGAGGGACTGTATAGCAGAACCCCTGGCTGGTAGCATCACAACACCTCCTCTGCTTATCG  
TATTTTATCAACAGCACTCTACCATCGATCCTATGTGGAATGTCCGCCACCTTGGTTCCAGT  
GCTGGAAAACGATATTACCTCAGTTTGTAAAGGCTGCCAAGTTACTCCATTGGAATGGACA  
TTTGAAGCCATGGGGAAGGACTGCTTCATATACTGATGTTTGGGGAAAAATGGTATATTCCA  
GACCCAACAGGCAAATTCAACCTAATCCGAAGATATACCGAGATCTCAAACATAAAGTGAAA  
CAGAATTTGAACTGTAAGCAAGCATTTCTCAGGAAGTCCTGGAAGATAGCATGCGTGGGAAG  
TAACAGTTGCTAGGCTTCAATGCCTATCGGTAGCAAGCCATGGAAAAAGATGTGTCAGCTAG  
GTAAAGATGACAACTGCCCTGTCTGGCAGTCAGCTTCCCAGACAGACTATAGACTATAAAT  
ATGTCTCCATCTGCCTTACCAAGTGTCTTCTTACTACAATGCTGAATGACTGGAAAGAAGAA  
CTGATATGGCTAGTTCAGCTAGCTGGTACAGATAATTCAAACTGCTGTTGGTTTTAATTTT  
GTAACCTGTGGCCTGATCTGTAAATAAACTTACATTTTTCAATAGGTAAAAAAAAAAAAA  
AAAAAA

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FIGURE 108

CTGCAGGTAGACATCTCCACTGCCCAGGAATCACTGAGCGTGCAGACAGCACAGCCTCCTCT  
GAAGGCCGCGCCATACCAGAGTCCTGCCTCGGCATGGGCCTCACCATTGAGGCAGCTCCACTG  
TCTGTGCTGGTCTGAGGGTGCTGCCTGTCAATGGGGGCAGCCATCTCCCAGGGGGCCCTCATC  
GCCATCGTCTGCAACGGTCTCGTGGGCTTCTTGCTGCTGCTGCTCTGGGTCACTCCTCTGCTG  
GGCCTGCCATTCTCGTCTGCCGACGTTGACTCTCTCTCTGAATCCAGTCCCAACTCCAGCCC  
TGGCCCCCTGTCTGAGAAGGCCCCACCACCCCAGAAGCCCAGCCATGAAGGCAGCTACCTGC  
TGCAGCCCTGAAGGCCCCCTGGCCTAGCCTGGAGCCCAGGACCTAAGTCCACCTCACCTAGAG  
CCTGGAATTAGGATCCCAGAGTTCAGCCAGCCTGGGGTCCAGAACTCAAGAGTCCGCCCTGCT  
TGGAGCTGGACCCAGCGGCCCAGAGTCTAGCCAGCTTGGCTCCAATAGGAGCTCAGTGGCCC  
TAAGGAGATGGGCCTGGGGTGGGGGCTTATGAGTTGGTGCTAGAGCCAGGGCCATCTGGACT  
ATGCTCCATCCCAAGGGCCAAGGGTCAGGGGCCGGGTCCACTCTTTCCCTAGGCTGAGCACC  
TCTAGGCCCTCTAGGTTGGGGAAGCAAACCTGGAACCCATGGCAATAATAGGAGGGTGTCCAG  
GCTGGGGCCCCTCCCCTGGTCCTCCAGTGTTTGCTGGATAATAAATGGAACCTATGGCTCTAA  
AAAAAAAAAAAAAAAAAAAA



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FIGURE 109

MGAAISQGALIAIVCNGLVGFLLLLLWVILCWACHSRLPTLTLSLNPVPTPALAPVLRPHH

PRSPAMKAATCCSPEGPWPSLEPRT

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FIGURE 110

GTTTGAATTCCTTCAACTATACCCACAGTCCAAAAGCAGACTCACTGTGTCCCAGGCTACCA  
GTTCCCTCCAAGCAAGTCATTTCCCTTATTTAACCGATGTGTCCCTCAAACACCTGAGTGCTA  
CTCCCTATTTGCATCTGTTTTGATAAATGATGTTGACACCCTCCACCGAATTCTAAGTGGAA  
TCATGTCGGAAGAGATACAATCCTTGGCCTGTGTATCCTCGCATTAGCCTTGTCTTTGGCC  
ATGATGTTTACCTTCAGATTCATCACCACCCTTCTGGTTCACATTTTCATTTTATTGGTTAT  
TTTGGGATTGTTGTTTGTCTGCGGTGTTTTATGGTGGCTGTATTATGACTATACCAACGACC  
TCAGCATAGAATTGGACACAGAAAGGGAAAATATGAAGTGCCTGCTGGGGTTTGCTATCGTA  
TCCACAGGCATCACGGCAGTGCTGCTCGTCTTGATTTTTGTTCTCAGAAAGAGAATAAAATT  
GACAGTTGAGCTTTTCCAAATCACAAATAAAGCCATCAGCAGTGCTCCCTTCCTGCTGTTCC  
AGCCACTGTGGACATTTGCCATCCTCATTTTCTTCTGGGTCCTCTGGGTGGCTGTGCTGCTG  
AGCCTGGGAACTGCAGGAGCTGCCCAGGTTATGGAAGGCGGCCAAGTGGAATATAAGCCCCCT  
TTCGGGCATTTCGGTACATGTGGTTCGTACCATTTAATTGGCCTCATCTGGACTAGTGAATTCA  
TCCTTGCGTGCCAGCAAATGACTATAGCTGGGGCAGTGGTTACTTGTTATTTCAACAGAAGT  
AAAAATGATCCTCCTGATCATCCCATCCTTTTCGTCTCTCTCCATTCTCTTCTTCTACCATCA  
AGGAACCGTTGTGAAAGGGTCATTTTAACTCTCTGTGGTGAGGATTCCGAGAATCATTGTCA  
TGTACATGCAAAACGCACTGAAAGAACAGCAGCATGGTGCATTGTCCAGGTACCTGTTCCGA  
TGCTGCTACTGCTGTTTTCTGGTGTCTTGACAAATACCTGCTCCATCTCAACCAGAATGCATA  
TACTACAACCTGCTATTAAATGGGACAGATTTCTGTACATCAGCAAAAGATGCATTCAAATCT  
TGTCCAAGAACTCAAGTCACTTTACATCTATTAACTGCTTTGGGAGACTTCATAATTTTTCTA  
GGAAAGGTGTTAGTGGTGTGTTTCACTGTTTTTGGAGGACTCATGGCTTTTAACTACAATCG  
GGCATTCCAGGTGTGGGCAGTCCCTCTGTTATTGGTAGCTTTTTTTGCTACTTAGTAGCCC  
ATAGTTTTTTATCTGTGTTTGAAACTGTGCTGGATGCACTTTTCTGTGTTTTGCTGTTGAT  
CTGGAAACAAATGATGGATCGTCAGAAAAGCCCTACTTTATGGATCAAGAATTTCTGAGTTT  
CGTAAAAAGGAGCAACAAATTAAACAATGCAAGGGCACAGCAGGACAAGCACTCATTAAGGA  
ATGAGGAGGGAACAGAACTCCAGGCCATTGTGAGATAGATACCCATTTAGGTATCTGTACCT  
GGAAACATTTCTTCTAAGAGCCATTTACAGAATAGAAGATGAGACCACTAGAGAAAAAGTT  
AGTGAATTTTTTTTTAAAAAGACCTAATAAACCTATTCTTCTCCTCAAAA

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FIGURE 111

MSGRDTILGLCILALALSLAMMFTFRFITTLVHIFISLVILGLLFVCGVLWWLYDYTNDL  
SIELDTERENMKCVLGFAIVSTGITAVLLVLIFVLRKRIKLTVELFQITNKAISSAPFLLFQ  
PLWTFAILIFFWVLWVAVLLSLGTAGAAQVMEGGQVEYKPLSGIRYMWSYHLIGLIWTSEFI  
LACQQMTIAGAVVTCYFNRSKNDDPDHPILSSLSILFFYHQGTVVKGSFLISVVRIPRIIVM  
YMQNALKEQQHGALSRYLFRCCYCCFWCLDKYLLHLNQNAAYTTTAINGTDFCTSAKDAFKIL  
SKNSSHFTSINCFGDFIIFLGKVLVVCFTVFGGLMAFNYNRAFQVWAVPLLLVAFFAYLVAH  
SFLSVFETVLDALFLCFAVDLETNDGSSEKPYFMDQEFLSFVKRSNKLNNARAQQDKHSLRN  
EEGTELQAIVR

FIGURE 112

[illegible]

FIGURE 113

MRTVVLTMKASVIEMFLVLLVTGVHSNKETAKKIKRPKFTVPQINCDVKAGKIIDPEFIVKC  
PAGCQDPKYHVYGTDVYASYSSVCGAAVHSGVLDNSGGKILVRKVAGQSGYKGSYSNGVQSL  
SLPRWRESFIVLESKPKKGVITYPSALTYSSSKSPAAQAGETTKAYQRPPIPGTTAQPVTLMQ  
LLAVTVAVATPTTLPRPSPSAASTTIPRPQSVGHRSQEMDLWSTATYTTSSQNRPRADPGIQ  
RQDPGAAAFQKPVGADVSLGLVPKEELSTQSLEPVSLGDPNCKIDLSFLIDGSTSIGKRRFR  
IQKQLLADVAQALDIGPAGPLMGVVQYGDNPATHFNLKTHTNSRDLKTAIEKITQRGGLSNV  
GRAISFVTKNFFSKANGNRSGAPNVVVVMVDGWPTDKVEEASRLARESGINIFFITIEGAAE  
NEKQYVVEPNFANKAVCRTNGFYSLHVQSWFGLHKTLLQPLVKRVCDTDRILACSKTCLNSADI  
GFVIDGSSSVGTGNFRTVLQFVTNLTKFEISDTRIGAVQYTYEQRLFEFGFDKYSSKPD  
LNAIKRVGYWSGGTSTGAAINFALQFLFKSKPNKRKLMILITDGRSYDDVRIPAMAAHLKG  
VITYAIGVAWAAQEELEVIATHPARDHSFFVDEFNLHQYVPRIIQNICTEFNSQPRN

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FIGURE 114

CAGGATGAACTGGTTGCAGTGGCTGCTGCTGCTGCGGGGGCGCTGAGAGGACACGAGCTCTA  
TGCCCTTTCCGGCTGCTCATCCCGCTCGGCCTCCTGTGCGCGCTGCTGCCCTCAGCACCATGGT  
GCGCCAGGTCCCGACGGCTCCGCGCCAGATCCCGCCCACTACAGTTTTTCTCTGACTCTAAT  
TGATGCACTGGACACCTTGCTGATTTTGGGGAATGTCTCAGAATTCCAAAGAGTGGTTGAAG  
TGCTCCAGGACAGCGTGGACTTTGATATTGATGTGAACGCCTCTGTGTTTGAACAAACATT  
CGAGTGGTAGGAGGACTCCTGTCTGCTCATCTGCTCTCCAAGAAGGCTGGGGTGGAAGTAGA  
GGCTGGATGGCCCTGTTCCGGGCCTCTCCTGAGAAATGGCTGAGGAGGCGGCCCCGAAACTCC  
TCCCAGCCTTTAGACCCCCACTGGCATGCCATATGGAACAGTGAACCTTACTTCATGGCGTG  
AACCCAGGAGAGACCCCTGTACCTGTACGGCAGGGATTGGGACCTTCATTGTTGAATTTGC  
CACCTGAGCAGCCTCACTGGTGACCCGGTGTTTGAAGATGTGGCCAGAGTGGCTTTGATGC  
GCCTCTGGGAGAGCCGGTCAGATATCGGGCTGGTCGGCAACCACATTGATGTGCTCACTGGC  
AAGTGGGTGGCCAGGACGCAGGCATCGGGCTGGCGTGGACTCCTACTTTGAGTACTTGGT  
GAAAGGAGCCATCCTGCTTCAAGATAAGAAGCTCATGGCCATGTTCTAGAGTATAACAAAG  
CCATCCGGAACCTACACCCGCTTCGATGACTGGTACCTGTGGGTTCAGATGTACAAGGGGACT  
GTGTCCATGCCAGTCTTCCAGTCTTGGAGGCCTACTGGCCTGGTCTTCAGAGCCTCATTGG  
AGACATTGACAATGCCATGAGGACCTTCCTCAACTACTACACTGTATGGAAGCAGTTTGGGG  
GGCTCCCGGAATTCTACAACATTCCTCAGGGATACACAGTGGAGAAGCGAGAGGGCTACCCA  
CTTCGGCCAGAACTTATTGAAAGCGCAATGTACCTCTACCGTGCCACGGGGGATCCCACCCT  
CCTAGAACTCGGAAGAGATGCTGTGGAATCCATTGAAAAAATCAGCAAGGTGGAGTGC GGAT  
TTGCAACAATCAAAGATCTGCGAGACCACAAGCTGGACAACCGCATGGAGTCGTTCTTCCTG  
GCCGAGACTGTGAAATACCTCTACCTCCTGTTTGACCCAACCAACTTCATCCACAACAATGG  
GTCCACCTTCGACGCGGTGATCACCCCTATGGGGAGTGCATCCTGGGGGCTGGGGGTACA  
TCTTCAACACAGAAGCTCACCCCATCGACCTTGCCGCCCTGCACTGCTGCCAGAGGCTGAAG  
GAAGAGCAGTGGGAGGTGGAGGACTTGATGAGGGAATTCTACTCTCTCAAACGGAGCAGGTC  
GAAATTTAGAAAAACACTGTTAGTTTCGGGGCCATGGGAACCTCCAGCAAGGCCAGGAACAC  
TCTTCTCACCAGAAAACCATGACCAGGCAAGGGAGAGGAAGCCTGCCAAACAGAAGGTCCCA  
CTTCTCAGCTGCCCCAGTCAGCCCTTCACCTCCAAGTTGGCATTACTGGGACAGGTTTTCTT  
AGACTCCTCATAAACCCTGGATAATTTTTTTATTTTTATTTTTTTGAGGCTAAACTATAATA  
AATTGCTTTTGGCTATCATAAAA

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FIGURE 115

MPFRLLIPLGLLCALLPQHGGAPGPDGSAPDPAHYSFSLTLIDALDTLLILGNVSEFQRVVE  
VLQDSVDFDIDVNASVFETNIRVVGGLLSAHLSSKKAGVEVEAGWPCSGPLLRMAEEAARKL  
LPAFQTPTGMPYGTVNLLHGVNPGETPVTCTAGIGTFIVEFATLSSLTGDPVFEDVARVALM  
RLWESRSDIGLVGNHIDVLTGKWVAQDAGIGAGVDSYFEYLVKGAILLQDKKLMAMFLEYNK  
AIRNYTRFDDWYLVWQMYKGTVMSPVFSLEAYWPGLQSLIGDIDNAMRTFLNYYTVWKQFG  
GLPEFYNI PQGYTVEKREGYPLRPELIESAMYLYRATGDPPTLLELGRDAVESIEKISKVECG  
FATIKDLRDHKL DNRMESFFLAETVKYLYLLFDPTNF IHNNGSTFDAVITPYGECILGAGGY  
IFNTEAHPIDLAALHCCQRLKEEQWEVEDLMREFYSLKRSRSKFQKNTVSSGPWEPPARPGT  
LFSPENHDQARERKPAKQKVPLLSCPSQPFTSKLALLGQVFLDSS

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FIGURE 116

AAAGTTACATTTTCTCTGGAACCTCTCCTAGGCCACTCCCTGCTGATGCAACATCTGGGTTTG  
GGCAGAAAGGAGGGTGCTTCGGAGCCCCGCCCTTTCTGAGCTTCCTGGGCCGGCTCTAGAACA  
ATTGAGGCTTCGCTGCGACTCAGACCTCAGCTCCAACATATGCATTCTGAAGAAAGATGGCT  
GAGATGGACAGAATGCTTTATTTTGGAAAGAAACAATGTTCTAGGTCAAACCTGAGTCTACCA  
AATGCAGACTTTCACAATGGTTCTAGAAGAAATCTGGACAAGTCTTTTCATGTGGTTTTCT  
ACGCATTGATTCCATGTTTGCTCACAGATGAAGTGGCCATTCTGCCTGCCCCCTCAGAACCTC  
TCTGTACTCTCAACCAACATGAAGCATCTCTTGATGTGGAGCCCAGTGATCGCGCCTGGAGA  
AACAGTGTAATACTGTCGAATACCAGGGGGAGTACGAGAGCCTGTACACGAGCCACATCT  
GGATCCCCAGCAGCTGGTGCTCACTCACTGAAGGTCTTGAGTGTGATGTCACTGATGACATC  
ACGGCCACTGTGCCATACAACCTTCGTGTCAGGGCCACATTGGGCTCACAGACCTCAGCCTG  
GAGCATCCTGAAGCATCCCTTTAATAGAACTCAACCATCCTTACCCGACCTGGGATGGAGA  
TCACCAAAGATGGCTTCCACCTGGTTATTGAGCTGGAGGACCTGGGGCCCCAGTTTGAGTTC  
CTTGTTGGCCTACTGGAGGAGGGAGCCTGGTGCCGAGGAACATGTCAAAATGGTGAGGAGTGG  
GGGTATTCCAGTGACCTAGAAACCATGGAGCCAGGGGCTGCATACTGTGTGAAGGCCCAGA  
CATTCGTGAAGGCCATTGGGAGGTACAGCGCCTTCAGCCAGACAGAATGTGTGGAGGTGCAA  
GGAGAGGCCATTCCCCTGGTACTGGCCCTGTTTGCTTTGCTTTGCTTTCATGCTGATCCTTGT  
GGTCGTGCCACTGTTTCGTCTGGAATGGGCCGGCTGCTCCAGTACTCCTGTTGCCCGTGG  
TGGTCTCCAGACACCTTGAAAATAACCAATTCACCCAGAAAGTTAATCAGCTGCAGAAGG  
GAGGAGGTGGATGCCTGTGCCACGGCTGTGATGTCTCCTGAGGAACTCCTCAGGGCCTGGAT  
CTCATAGGTTTGCAGGAGGGCCAGGTGAAGCCGAGAACCTGGTCTGCATGACATGGAAACC  
ATGAGGGGACAAGTTGTGTTTCTGTTTTCCGCCACGGACAAGGGATGAGAGAAGTAGGAAGA  
GCCTGTTGTCTACAAGTCTAGAAGCAACCATCAGAGGCAGGGTGGTTTGTCTAACAGAACAC  
TGACTGAGGCTTAGGGGATGTGACCTCTAGACTGGGGGCTGCCACTTGCTGGCTGAGCAACC  
CTGGGAAAAGTGACTTCATCCCTTCGGTCCTAAGTTTTCTCATCTGTAATGGGGGAATTACC  
TACACACCTGCTAAACACACACACAGAGTCTCTCTATATATACACACGTACACATAAA  
TACACCCAGCACTTGCAAGGCTAGAGGGAACTGGTGACACTCTACAGTCTGACTGATTGAG  
TGTTTCTGGAGAGCAGGACATAAATGTATGATGAGAATGATCAAGGACTCTACACACTGGGT  
GGCTTGAGAGCCCACTTTCCAGAAATAATCCTTGAGAGAAAAGGAATCATGGGAGCAATGG  
TGTTGAGTTCACTTCAAGCCCAATGCCGGTGAGAGGGGAATGGCTTAGCGAGCTCTACAGT  
AGGTGACCTGGAGGAAGGTACAGCCACACTGAAAATGGGATGTGCATGAACACGGAGGATC  
CATGAACTACTGTAAAGTGTGACAGTGTGTGCACACTGCAGACAGCAGGTGAAATGTATGT  
GTGCAATGCGACGAGAATGCAGAAGTCAGTAACATGTGCATGTTTGTGTGCTCCTTTTTTC  
TGTTGGTAAAGTACAGAATTGAGCAATAAAAAGGGCCACCCTGGCCAAAAGCGGTAAAAAA  
AAAAAAAAA



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FIGURE 117

MQTFTMVLEEIWTSLFMWFFYALIPCLLTDEVAILPAPQNLSVLSTNMKHELLMWSPVIAPGE  
TVYYSVEYQGEYESLYTSHIWIPSSWCSLTEGPECDDITATVPYNLRVRATLGSQTS  
SILKHPFNRNSTILTRPGMEITKDGFLVIELEDLGPQFEFLVAYWRREPGAEEHVKMVRSG  
GIPVHLETMEPGAAYCVKAQTFVKAIGRYSAFSQTECVQGEAIPLVLALFAFVGFMILV  
VVPLFVWKMGRLLQYSCCPVVVLPDTLKITNSPQKLISCRREEVDACATAVMSPEELLRAWIS

**Important features:**

**Signal peptide:**

amino acids 1-29

**Transmembrane domain:**

amino acids 230-255

**N-glycosylation sites.**

amino acids 40-43 and 134-137

**Tissue factor proteins homology.**

amino acids 92-119

**Integrins alpha chain protein homology.**

amino acids 232-262

FIGURE 118

TCCTGCTGATGCACATCTGGGTTTGGCAAAGGAGGTTGCTTCGAGCCGCCCTTTCTAGCTT  
CCTGGCCGGCTCTAGAACAATTGAGGCTTCGCTGCGACTAGACCTCAGCTCCAACATATGCA  
TTCTGAAGAAAGATGGCTGAGATGACAGAATGCTTTATTTTGGAAAGAAACAATGTTCTAGG  
TCAAACCTGAGTCTACCAAATGCAGACTTTCACAATGGTTCTAGAAGAAATCTGGACAAGTCT  
TTTCATGTGGTTTTTCTACGCATTGATTCCATGTTTGCTCACAGATGAAGTGGCCATTCTGC  
CTGCCCCCTCAGAACCTCTCTGTACTCTCAACCAACATGAAGCATCTCTTGATGTGGAGCCCA  
GTGATCGCGCCTGGAGAAACAGTGTACTATTCTGTGGAATACCAGGGGGAGTACGAGAGCCT  
GTACACGAGCCACATCTGGATCCCCAGCAGCTGGTGCTCACTCACTGAAGGTCCTGAGTGTG  
ATGTCACTGATGACATCACGGCCACTGTGCCATACAACCTTTGTGTGAGGGCCACATTGGGC  
TCACAGACCTCAGCCTGGAGCATCCTGAAGCATCCCTTTAATAGAAACTCAACCATCCTTAC  
CCGACCTGGGATGGAGATCACCAAAGATGGCTTNCACCTGGTTATTGAGCTGGAGGACCTGG  
GGCCCCAGTTTGAGTTCCTTGTGGCCTANTGGAGGAGGGGCGAACCCCTTGCGGCGCAAGGG  
GTTNGCGAACCCCTTGCGGCCGCTGGGGTATCTCTCGAGAAAAGAGAGGCCCAATATGACCCAC  
ATACTCAATATGGACGAANTGCTATTGTCCACCTGTTTGAGTGGCGCTGGGTTGAT

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FIGURE 119

CGGACGCGTGGGCCGCCACCTCCGGAACAAGCCATGGTGGCGGCGACGGTGGCAGCGGCGTG  
GCTGCTCCTGTGGGCTGCGGCCTGCGCGCAGCAGGAGCAGGACTTCTACGACTTCAAGGCGG  
TCAACATCCGGGGCAAACCTGGTGTGCTGGAGAAGTACCGCGGATCGGTGTCCCTGGTGGTG  
AATGTGGCCAGCGAGTGC GGCTTCACAGACCAGCACTACCGAGCCCTGCAGCAGCTGCAGCG  
AGACCTGGGCCCCCACCCTTTAACGTGCTCGCCTTCCCCTGCAACCAGTTTGGCCAACAGG  
AGCCTGACAGCAACAAGGAGATTGAGAGCTTTGCCCCGCCGACCTACAGTGTCTCATTCCCC  
ATGTTTAGCAAGATTGCAGTCACCGGTACTGGTGCCCATCCTGCCTTCAAGTACCTGGCCCA  
GACTTCTGGGAAGGAGCCCACCTGGAACCTTCTGGAAGTACCTAGTAGCCCCAGATGGAAGG  
TGGTAGGGGCTTGGGACCCAACTGTGTCAGTGGAGGAGGTCAGACCCAGATCACAGCGCTC  
GTGAGGAAGCTCATCCTACTGAAGCGAGAAGACTTATAAACCACCGCGTCTCCTCCTCCACCA  
CCTCATCCCGCCCACCTGTGTGGGGCTGACCAATGCAAACCTCAAATGGTGCTTCAAAGGGAG  
AGACCCACTGACTCTCCTTCCTTTACTCTTATGCCATTGGTCCCATCATTCTTGTGGGGGAA  
AAATTCTAGTATTTTGATTATTTGAATCTTACAGCAACAAATAGGAACTCCTGGCCAATGAG  
AGCTCTTGACCAGTGAATCACCAGCCGATACGAACGTCTTGCCAACAAAAATGTGTGGCAA  
TAGAAGTATATCAAGCAATAATCTCCCACCCAAGGCTTCTGTAAACTGGGACCAATGATTAC  
CTCATAGGGCTGTTGTGAGGATTAGGATGAAATACCTGTGAAAGTGCCTAGGCAGTGCCAGC  
CAAATAGGAGGCATTCAATGAACATTTTTTGCATATAAACCAAAAAATAACTTGTATCAAT  
AAAACTTGCAATCCAACATGAATTTCCAGCCGATGATAATCCAGGCCAAAGGTTTAGTTGTT  
GTTATTTCTCTGTATTATTTTCTTCATTACAAAAGAAATGCAAGTTCATTGTAACAATCCA  
AACAAATACCTCACGATATAAAATAAAAAATGAAAGTATCCTCCTCAAAAA

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**FIGURE 120**

MVAATVAAAWLLLWAAACAQQEQDFYDFKAVNIRGKLVSLEKYRGSVSLVVNVASECGFTDQ  
HYRALQQQLQRDLGPHHFNVLAFPCNQFGQQEPDSNKEIESFARRTYSVSFPMFSKIAVTGTG  
AHPAFKYLAQTSGKEPTWNFWKYL VAPDGKVVGAWDPTVSVEEVRPQITALVRKLILLKREDL

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FIGURE 121

CGGACGCGTGGGCGGGCCGGGACGCAGGGCAAAGCGAGCCATGGCTGTCTACGTCGGGATGC  
TGCGCCTGGGGAGGCTGTGCGCCGGGAGCTCGGGGGTGCTGGGGGCCCGGGCGCCCTCTCT  
CGGAGTTGGCAGGAAGCCAGGTTGCAGGGTGTCCGCTTCCTCAGTTCAGAGAGGTGGATCG  
CATGGTCTCCACGCCCATCGGAGGCCTCAGCTACGTTTCAGGGGTGCACCAAAAAGCATCTTA  
ACAGCAAGACTGTGGGCCAGTGCTTGAGACCACAGCACAGAGGGTCCCAGAACGAGAGGGCC  
TTGGTCTGCTCCATGAAGACGTCAGGTTGACCTTTGCCCAACTCAAGGAGGAGGTGGACAA  
AGCTGCTTCTGGCCTCCTGAGCATTGGCCCTTGCAAAGGTGACCGGCTGGGCATGTGGGGAC  
CTAACTCCTATGCATGGGTGCTCATGCAGTTGGCCACCGCCAGGCGGGCATCATTTCTGGTG  
TCTGTGAACCCAGCCTACCAGGCTATGGAAGTGGAGTATGTCCTCAAGAAGGTGGGCTGCAA  
GGCCCTTGTTGTTCCCAAGCAATTCAAGACCCAGCAATACTACAACGTCCTGAAGCAGATCT  
GTCCAGAAGTGGAGAATGCCAGCCAGGGGCCCTGAAGAGTCAGAGGCTCCCAGATCTGACC  
ACAGTCATCTCGGTGGATGCCCCCTTTGCCGGGGACCCTGCTCCTGGATGAAGTGGTGGCGGC  
TGGCAGCACACGGCAGCATCTGGACCAGCTCCAATACAACCAGCAGTTCTGTCTCTGCCATG  
ACCCCATCAACATCCAGTTCACCTCGGGGACAACAGGCAGCCCCAAGGGGGCCACCCTCTCC  
CACTACAACATTGTCAACAACCTCAACATTTTAGGAGAGCGCCTGAAACTGCATGAGAAGAC  
ACCAGAGCAGTTGCGGATGATCCTGCCCAACCCCTGTACCATTGCCCTGGGTTCCTGTGGCAG  
GCACAATGATGTGTCTGATGTACGGTGCCACCCTCATCCTGGCCTCTCCCATCTTCAATGGC  
AAGAAGGCAGTGGAGGCCATCAGCAGAGAGAGAGGCACCTTCCTGTATGGTACCCCCACGAT  
GTTCTGTGGACATTCTGAACCAGCCAGACTTCTCCAGTTATGACATCTCGACCATGTGTGGAG  
GTGTCAATTGCTGGGTCCCCTGCACCTCCAGAGTTGATCCGAGCCATCATCAACAAGATAAAT  
ATGAAGGACCTGGTGGTTGCTTATGGAACCAAGAGAACAGTCCCGTGACATTCGCGCACTT  
CCCTGAGGACACTGTGGAGCAGAAGGCAGAAAGCGTGGGCAGAAATTATGCCTCACACGGAGG  
CCCGGATCATGAACATGGAGGCAGGGACGCTGGCAAAGCTGAACACGCCCGGGGAGCTGTGC  
ATCCGAGGGTACTGCGTCATGCTGGGCTACTGGGGTGAGCCTCAGAAGACAGAGGAAGCAGT  
GGATCAGGACAAGTGGTATTGGACAGGAGATGTCGCCACAATGAATGAGCAGGGCTTCTGCA  
AGATCGTGGGCCGCTCTAAGGATATGATCATCCGGGGTGGTGAGAACATCTACCCCGCAGAG  
CTCGAGGACTTCTTTCACACACACCCGAAGGTGCAGGAAGTGCAGGTGGTGGGAGTGAAGGA  
CGATCGGATGGGGGAAGAGATTTGTGCCTGCATTGGCTGAAGGACGGGGAGGAGACCACGG  
TGGAGGAGATAAAAGCTTTCTGCAAAGGGAAGATCTCTCACTTCAAGATTCGGAAGTACATC  
GTGTTTGTCAAAACTACCCCTCACCATTTTCAGGAAAGATCCAGAAATTCAAACCTTCGAGA  
GCAGATGGAACGACATCTAAATCTGTGAATAAAGCAGCAGGCCTGTCTGGCCGGTTGGCTT  
GACTCTCTCCTGTGAGAATGCAACCTGGCTTTATGCACCTAGATGTCCCAGCACCCAGTTT  
TGAGCCAGGCACATCAAATGTCAAGGAATTGACTGAACGAACTAAGAGCTCCTGGATGGGTC  
CGGGAACTCGCCTGGGCACAAGGTGCCAAAAGGCAGGCAGCCTGCCAGGCCCTCCCTCCTG  
TCCATCCCCACATTCCCCTGTCTGTCTTGTGATTTGGCATAAAGAGCTTCTGTTTTCTTT  
GAAAAAAAAAAAAAAAAA

FIGURE 122

MAVYVGMLRLGRLCAGSSGVLGARAALSRWQEARLQGVRFLSSREVD RMVSTPIGGLSYVQ  
GCTKKHLNSKTVGQCLETTAQRVPEREALVVLHEDVRLTFAQLKEEVDKAASGLLSIGLCKG  
DRLGMWGPN SYAWVLMQLATAQAGIILVSVNPAYQAMELEYVLKKVGCKALVFPKQFKTQQY  
YNVLKQICPEVENA QPGALKSQRLPDLTTVISVDAPLPGTLLLDEVVAAGSTRQHLDQLQYN  
QQFLSCHDPINIQFTSGTTGSPKGATLSHYNIVNNSNILGERLKLHEKTPEQLRMILPNPLY  
HCLGSVAGTMMCLMYGATLILASPIFNGKKALEAISRERGTFLYGTPTMFVDILNQPDFSSY  
DISTMCGGVIAGSPAPPELIRAIINKINMKDLVVAYGTTENSPVTFAHFPEDTVEQKAESVG  
RIMPHTEARIMNMEAGTLAKLNTPGELCIRGYCVMLGYWGEPQKTEEAVDQDKWYWTGDVAT  
MNEQGFC KIVGRSKDMIIRGGENIYPAELEDFHHTHPKVQEVQVVGVKDDRMGEEICACIRL  
KDGEETTVEEIKAFCKGKISHFKIPKYIVFVTNYPLTISGKIQFKLREQMERHLNL

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FIGURE 123

CAACTCCAACATTTTAGGAGAGCGCCTGAAACTGCATGAGAAGACACCAGAGCAGTTGCGGA  
TGATCCTGCCCCAACCCCTGTACCATTCCTGGGTTCCGTGGCAGGCACAATGATGTGTCTG  
ATGTACGGTGCCACCCTCATCCTGGCCTCTCCCATCTTCAATGGCAAGAAGGCACTGGAGGC  
CATCAGCAGAGAGAGAGAGGCACCTTCCTGTATGGTACCCCCACGATGTTTCGTGGACATTCTGA  
ACCAGCCAGACTTCTCCAGTTATGACATCTCGACCATGTGTGGAGGTGTCATTGCTGGGTCC  
CCTGCACCTCCAGAGTTGATCCGAGCCATCATCAACAAGATAAATATGAAGGACCTGGTGGT  
TGCTTATGGAACCACAGAGAACAGTCCCGTGACATTCGCGCACTTCCCTGAGGACACTGTGG  
AGCAGAAAGGCAGAAAGCGTGGGCAGAATTATGCCTCACACGGAGGCGCGGATCATGAACATG  
GAGGCAGGGACGCTGGCAAAGCTGAACACGCCCCGGGGAGCTGTGCATCCGAGGGTACTGCGT  
CATGCTGGGCTACTGGGGTGAGCCTCAGAAGACAGAGGAAGCAGTGGATCAGGACAAGTGGT  
ATTGGACAGGAGATGTGCCAC

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FIGURE 124

GAGCAGGACGGAGCCATGGACCCCGCCAGGAAAGCAGGTGCCAGGCCATGATCTGGACTGC  
AGGCTGGCTGCTGCTGCTGCTGCTTCGCGGAGGAGCGCAGGCCCTGGAGTGCTACAGCTGCG  
TGCAGAAAGCAGATGACGGATGCTCCCCGAACAAGATGAAGACAGTGAAGTGCGCGCCGGGC  
GTGGACGTCTGCACCGAGGCCGTGGGGGCGGTGGAGACCATCCACGGACAATTCTCGCTGGC  
AGTGCGGGGTTGCGGTTCTGGGACTCCCCGGCAAGAATGACCGCGGCCTGGATCTTCACGGGC  
TTCTGGCGTTCATCCAGCTGCAGCAATGCGCTCAGGATCGCTGCAACGCCAAGCTCAACCTC  
ACCTCGCGGGCGCTCGACCCGGCAGGTAATGAGAGTGATACCCGCCCCAACGGCGTGGAGTG  
CTACAGCTGTGTGGGCCTGAGCCGGGAGGCGTGCCAGGGTACATCGCCGCGCGGTGCTGAGCT  
GCTACAACGCCAGCGATCATGTCTACAAGGGCTGCTTCGACGGCAACGTACCTTGACGGCA  
GCTAATGTGACTGTGTCCTTGCTGTCCGGGGCTGTGTCCAGGATGAATTCTGCACTCGGGA  
TGGAGTAACAGGCCCAGGGTTCACGCTCAGTGGCTCCTGTTGCCAGGGGTCCCGCTGTAAC  
CTGACCTCCGCAACAAGACCTACTTCTCCCTCGAATCCCACCCCTTGTCGGGCTGCCCCCT  
CCAGAGCCCACGACTGTGGCCTCAACCACATCTGTCACCACTTCTACCTCGGCCCCAGTGAG  
ACCCACATCCACCACCAACCCATGCCAGCGCCAACCAGTCAGACTCCGAGACAGGGAGTAG  
AACACGAGGCCTCCCGGGATGAGGAGCCCAGGTTGACTGGAGGCGCCGCTGGCCACCAGGAC  
CGCAGCAATTACAGGGCAGTATCCTGCAAAAGGGGGCCCCAGCAGCCCCATAATAAAGGCTG  
TGTGGCTCCACAGCTGGATTGGCAGCCCTTCTGTTGGCCGTGGCTGCTGGTGTCTACTGT  
GAGCTTCTCCACCTGGAAATTTCCCTCTCACCTACTTCTCTGGCCCTGGGTACCCCTCTTCT  
CATCACTTCTGTTCCACCACTGGACTGGGCTGGCCCAGCCCCTGTTTTTCCAACATTCCC  
CAGTATCCCCAGCTTCTGCTGCGCTGGTTTTCGGCTTTGGGAAATAAAATACCGTTGTATAT  
ATTCTGCCAGGGGTGTTCTAGCTTTTTTGAGGACAGCTCCTGTATCCTTCTCATCCTTGTCTC  
TCCGCTTGTCCTCTTGTGATGTTAGGACAGAGTGAGAGAAGTCAGCTGTACGGGGAAGGTG  
AGAGAGAGGATGCTAAGCTTCCTACTCACTTTCTCCTAGCCAGCCTGGACTTTGGAGCGTGG  
GGTGGGTGGGACAATGGCTCCCCACTCTAAGCACTGCCTCCCCTACTCCCCGCATCTTTGGG  
GAATCGGTTCCCCATATGTCTTCCTTACTAGACTGTGAGCTCCTCGAGGGGGGGCCCGGTAC  
CCAATTCGCCCTATAGTGAGTCGTA



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FIGURE 125

MDPARKAGAQAAMIWTAGWLLLLLLRGGQAQALECYSCVQKADDGCSPNKMKTVKCAPGVDVCT  
EAVGAVETIHGQFSLAVRGCGSGLPGKNDRGLDLHGLLAFIQLQQCAQDRCNALNLTSRAL  
DPAGNESAYPPNGVECYSCVGLSREACQGTSPPVVSCYNASDHVYKGCDFGNVTLTAANVTV  
SLPVRGCVQDEFCTRDGVTGPGFTLSGSCCQGSRCNSDLRNKTYFSPIPLVRLPPPEPTT  
VASTTSVT'TSTSAVRPTSTTKPMPAPTSQTTPRQGEHEASRDEEPRLTGGAAGHQDRSNSG  
QYPAKGGPQQPHNKGCVAPTAGLAALLLAVAAGVLL

CGGGACTCGGCGGGTCTCTGGGAGTCTCGGAGGGGACCGGCTGTGCAGACGCCATGGAGT  
TGGTGCTGGTATTTCTCTCTGCAGCCTGCTGGCCCCATGGTCTTGGCCAGTGCAGCTGAAAAG  
GAGAAGGAACTGGACCCCTTTTTCATTATGATTACCAGACCCTGAGGATTGGGGGACTGGTGT  
CGCTGTGGTCTCTTCTCGGTTGGGATCCTCCTTATCCTAAGTCGCAGGTGCAAGTGCAGTT  
TCAATCAGAAGCCCCGGGCCCCAGGAGATGAGGAAGCCCAGGTGGAGAACCTCATCACCGCC  
AATGCAACAGAGCCCCAGAAGCAGAGAACTGAAGTGCAGCCATCAGGTGGAAGCCTCTGGAA  
CCTGAGGCGGCTGCTTGAACCTTTGGATGCAATGTGCATGCTTAAGAAAACCGCCACTTC  
AGCAACAGCCCTTTCCCCAGGAGAAGCCAAGAAGCTTGTGTGTCCCCACCCTATCCCCCTTA  
ACACCATTCTCCACCTGATGATGCAACTAACACTTGCCCTCCCCTGCAGCCTGCGGTCTCT  
GCCCACCTCCCGTGATGTGTGTGTGTGTGTGTGTGTGTGACTGTGTGTGTTTGCTAACTGTG  
GTCTTTGTGGCTACTTGTTTGTGGATGGTATTGTGTTTGTGTAGTGAACGTGGACTCGCTTT  
CCCAGGCAGGGGCTGAGCCACATGGCCATCTGCTCCTCCCCTGCCCCCTGGCCCTCCATCAC  
CTTCTGCTCCTAGGAGGCTGCTTGTGTGCCGAGACCAGCCCCCTCCCCTGATTTAGGGATGC  
GTAGGGTAAGAGACACGGGCAGTGGTCTTCAGTCGTCTTGGGACCTGGGAAGGTTTGCAGCAC  
TTTGTGCATCATTCTTCATGGACTCCTTTCAGTCCTTTAAACAAAAACCTTGCTTCCTTATCCC  
ACCTGATCCCAGTCTGAAGGTCTCTTAGCAACTGGAGATACAAAGCAAGGAGCTGGTGAGCC  
CAGCGTTGACGTGAGGCAGGCTATGCCCTTCCGTGGTTAATTTCTTCCCAGGGGCTTCCAG  
AGGAGTCCCCATCTGCCCCGCCCCCTTCACAGAGCGCCCGGGGATTCCAGGCCCAGGGCTTCT  
ACTCTGCCCCCTGGGGAATGTGTCCCCTGCATATCTTCTCAGCAATAACTCCATGGGCTCTGG  
GACCTTACCCCTTCCAACCTTCCCTGCTTCTGAGACTTCAATCTACAGCCAGCTCATCCAG  
ATGCAGACTACAGTCCCTGCAATTGGGTCTCTGGCAGGCAATAGTTGAAGGACTCCTGTTCC  
GTTGGGGCCAGCACACCGGGATGGATGGAGGGAGAGCAGAGGCCTTTGCTTCTCTGCCTACG  
TCCCCTTAGATGGGCAGCAGAGGCAACTCCCGCATCCTTTGCTCTGCCTGTGGTGGTTCAG  
GCGGTGAGCGAGGTGGGTTGGAGACTCAGCAGGCTCCGTGCAGCCCTTGGGAACAGTGAGAG  
GTTGAAGGTATAACGAGAGTGGGAACTCAACCCAGATCCCGCCCCCTCTGTCTCTGTGTT  
CCCGCGGAAACCAACCAAAACCGTGCGCTGTGACCCATTGCTGTTCTCTGTATCGTGATCTAT  
CCTCAACAACAACAGAAAAAGGAATAAAATATCCTTTGTTTCT

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**FIGURE 127**

MELVLVFLCSLLAPMVLASAAEKEKEMDPFHYDYQTLRIGGLVFAVVLFSVGILLILSRRCK  
CSFNQKPRAPGDDEEAQVENLITANATEPQKQRTQEVQPSGGSLWNLRLLEPLDANVDA

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**FIGURE 128**

AAACTTGACGCCATGAAGATCCCGGTCCTTCCTGCCGTGGTGCTCCTCTCCCTCCTGGTGCT  
CCTCTGCCCAGGGAGCCACCCTGGGTGGTCCTGAGGAAGAAAGCACCATTGAGAATTATG  
CGTCACGACCCGAGGCCTTTAACACCCCGTTCTGAAATCGACAAATTGCGATCTGCGTTT  
AAGGCTGATGAGTTCTGAACTGGCAGCCCTCTTTGAGTCTATCAAAGGAAACTTCCTTT  
CCTCAACTGGGATGCCTTTCCTAAGCTGAAAGGACTGAGGAGCGCAACTCCTGATGCCAGT  
GACCATGACCTCCACTGGAAGAGGGGGCTAGCGTGAGCGCTGATTCTCAACCTACCATAACT  
CTTTCCTGCCTCAGGAACTCCAATAAAACATTTTCCATCCAAA

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FIGURE 129

MKIPVLPVAVLLSLLVLHSAQGATLGGPEEESTIENYASRPEAFNTPFLNIDKLRSFAKDE  
FLNWHALFESIKRKLPFLNWDAFPKLGKGLRSATPDAQ

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FIGURE 130

CAGTTCTGAAATCAATGGAGTTAATTTAGGGAATACAAACCAGCCATGGGGGTGGAGATTGC  
CTTTGCCTCAGTGATTCTCACCTGCCTCTCCCTTCTGGCAGCAGGAGTCTCCCAGGTTGTTC  
TTCTCCAGCCAGTTCCAACCTCAGGAGACAGGTCCCAAGGCCATGGGAGATCTCTCCTGTGGC  
TTTGCCGGCCACTCATGAGAGAGTGTTTTTGTGTAAAGTATTTTTTAGAATACTGTTGACTTCT  
TCATGATTTAATAACCATCCTTTGCGAAGTTTTATGAGGCTTTAGGGGAATGTCAACCCCTCA  
AATTTTTGTTATACTAGATGGCTTCCATTTACCCACCACTATTTTAAGGTCCCTTTATTTTT  
AGGTTCAAGGTTCAATTTGACTTGAGAAAGTGCCCTTCTGCAGCTTCATTGATTTTGTATTATC  
TTCATTAATTGTAACGATTAAAAAAGAATAAGAGCACGCAGACCTCTAGGAGAATATTT  
TATCCCTGGGTGCCCCTGACACATTTATGTAGTGATCCCACAAATGTGATTGTTAATTTAAA  
TGTTATTCTAATATTAGTACATTCAGTTGTGATGTAATATGAATAACCAGAATCTATTTCTT  
AAAAGTTTTGAGTATATTTTTCAACTAGATATTTGTATAGAAAGACTGAATAGTGATG

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FIGURE 131

MGVEIAFASVILTCLSLLAAGVSQVLLQPVPTQETGPKAMGDLSCGFAGHS

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FIGURE 132

GGGGAATCTGCAGTAGGTCTGCCGGCGATGGAGTGGTGGGCTAGCTCGCCGCTTCGGCTCTG  
GCTGCTGTTGTTCCCTCCTGCCCTCAGCGCAGGGCCGCCAGAAGGAGTCAGGTTCAAAATGGA  
AAGTATTTATTGACCAAATTAACAGGTCTTTGGAGAATTACGAACCATGTTCAAGTCAAAAC  
TGCAGCTGCTACCATGGTGTCTAGAGAAGAGGATCTAACTCCTTTCCGAGGAGGCATCTCCAG  
GAAGATGATGGCAGAGGTAGTCAGACGGAAGCTAGGGACCCACTATCAGATCACTAAGAACA  
GACTGTACCCGGGAAAATGACTGCATGTTCCCTCAAGGTGTAGTGGTGTGAGCACTTTATT  
TTGGAAGTGATCGGGCGTCTCCCTGACATGGAGATGGTGATCAATGTACGAGATTATCCTCA  
GGTTCCTAAATGGATGGAGCCTGCCATCCCAGTCTTCTCCTTCAGTAAGACATCAGAGTACC  
ATGATATCATGTATCCTGCTTGGACATTTTGGGAAGGGGGACCTGCTGTTTGGCCAATTTAT  
CCTACAGGTCTTGGACGGTGGGACCTCTTCAGAGAAGATCTGGTAAGGTCAGCAGCACAGTG  
GCCATGGAAAAAGAAAACTCTACAGCATATTTCCGAGGATCAAGGACAAGTCCAGAACGAG  
ATCCTCTCATTTCTTCTGTCTCGGAAAAACCCAAAACCTGTTGATGCAGAATACACCAAAAAC  
CAGGCCCTGGAAATCTATGAAAGATACCTTAGGAAAGCCAGCTGCTAAGGATGTCCATCTTGT  
GGATCACTGCAAATACAAGTATCTGTTTAATTTTCGAGGCGTAGCTGCAAGTTTCCGGTTTA  
AACACCTCTTCCTGTGTGGCTCACTTGTTTTCCATGTTGGTGATGAGTGGCTAGAATTCTTC  
TATCCACAGCTGAAGCCATGGGTCACTATATCCCAGTCAAACAGATCTCTCCAATGTCCA  
AGAGCTGTTACAATTTGTAAAAGCAAATGATGATGTAGCTCAAGAGATTGCTGAAAGGGGAA  
GCCAGTTTATTAGGAACCATTTGCAGATGGATGACATCACCTGTTACTGGGAGAACCTCTTG  
AGTGAATACTCTAAATTCCTGTCTTATAATGTAACGAGAAGGAAAGGTTATGATCAAATTAT  
TCCCAAAATGTTGAAAACGAACTATAGTAGTCATCATAGGACCATAGTCCTCTTTGTGGCA  
ACAGATCTCAGATATCCTACGGTGAGAAGCTTACCATAAGCTTGGCTCCTATACCTTGAATA  
TCTGCTATCAAGCCAAATACCTGGTTTTCTTATCATGCTGCACCCAGAGCAACTCTTGAGA  
AAGATTTAAAATGTGTCTAATACACTGATATGAAGCAGTTCAACTTTTGGATGAATAAGGA  
CCAGAAATCGTGAGATGTGGATTTTGAACCCAACTCTACCTTTCATTTTCTTAAGACCAATC  
ACAGCTTGTGCCTCAGATCATCCACCTGTGTGAGTCCATCACTGTGAAATTGACTGTGTCCA  
TGTGATGATGCCCTTTGTCCCATTATTTGGAGCAGAAAATTCGTCAATTTGGAAGTAGTACAA  
CTCATTTGCTGGAATTGTGAAATTATTCAGGCGTGATCTCTGTCACTTTATTTTAATGTAGG  
AAACCTTATGGGGTTTATGAAAAATACTTGGGGATCATTCTCTGAATGGTCTAAGGAAGCGG  
TAGCCATGCCATGCAATGATGTAGGAGTTCCTTTTTGTAAAACCATAAACTCTGTTACTCAG  
GAGGTTTCTATAATGCCACATAGAAAGAGGCCAATTGCATGAGTAATTATTGCAATTGGATT  
TCAGGTTCCCTTTTTGTGCCTTCATGCCCTACTTCTTAATGCCTCTCTAAAGCCAAA



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FIGURE 133

MEWWASSPLRLWLLLFLLP  
SAQGRQKESGSKWKVFI  
DQINRSLENYEPCSSQNC  
SCYHGVIE  
EDLTPFRGGISRKMAEV  
VRRKLGTHYQITKNRLY  
RENDCMFPSRCSGVEHF  
ILEVIGRLPD  
MEMVINVRDYPQVPKW  
MEPAIPVFSFSKTSEYH  
DIMYPAWTFWEGGPAV  
WPIYPTGLGRWDL  
FREDLVRSAQWPWKKN  
STAYFRGSRTSPERDPL  
ILLSRKNPKLVDAEYTK  
NQAWKSMKDT  
LGKPAAKDVHLVDHCK  
YKYLENFRGVAASFRFK  
HLFLCGSLVFHVGD  
EWLEFFYPQLKPWVH  
YIPVKTDLSNVQELLQ  
FVKANDDVAQEIAERGS  
QFIRNHLQMDDITCYW  
ENLLSEYSKFLSY  
NVTRRKG YDQII PKML  
KTEL

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FIGURE 134

CACCCCTCCATTTCTCGCCATGCCCCCTGCACTGCTCCTGATCCCTGCTGCCCTCGCCTCTT  
TCATCCTGGCCTTTGGCACCGGAGTGGAGTTCGTGCGCTTACCTCCCTTCGGCCACTTCTT  
GGAGGGATCCCGGAGTCTGGTGGTCCGGATGCCCGCCAGGGATGGCTGGCTGCCCTGCAGGA  
CCGCAGCATCCTTGCCCCCTGGCATGGGATCTGGGGCTCCTGCTTCTATTTGTTGGGCAGC  
ACAGCCTCATGGCAGCTGAAAGAGTGAAGGCATGGACATCCCGGTACTTTGGGGTCTTCAG  
AGGTCACTGTATGTGGCCTGCACTGCCCTGGCCTTGACAGCTGGTGATGCGGTACTGGGAGCC  
CATACCCAAAGGCCCTGTGTTGTGGGAGGCTCGGGCTGAGCCATGGGGCCACCTGGGTGCCGC  
TCCTCTGCTTTGTGCTCCATGTATCTCCTGGCTCCTCATCTTTAGCATCCTTCTCGTCTTT  
GACTATGCTGAGCTCATGGGCCTCAAACAGGTATACTACCATGTGCTGGGGCTGGGCGAGCC  
TCTGGCCCTGAAGTCTCCCGGGCTCTCAGACTCTTCTCCACCTGCGCCACCCAGTGTGTG  
TGGAGCTGCTGACAGTGCTGTGGGTGGTGCCTACCCTGGGCACGGACCGTCTCCTCCTTGCT  
TTCTCCTTACCCTCTACCTGGGCCTGGCTCACGGGCTTGATCAGCAAGACCTCCGCTACCT  
CCGGGCCCAGCTACAAAGAAACTCCACCTGCTCTCTCGGCCCCAGGATGGGGAGGCAGAGT  
GAGGAGCTCACTCTGGTTACAAGCCCTGTTCTTCTCTCCCACTGAATTCTAAATCCTTAAC  
ATCCAGGCCCTGGCTGCTTCATGCCAGAGGCCCAAATCCATGGACTGAAGGAGATGCCCCCTT  
CTACTACTTGAGACTTTATTCTCTGGGTCCAGCTCCATACCCTAAATTCTGAGTTTCAGCCA  
CTGAACTCCAAGGTCCACTTCTCACCAGCAAGGAAGAGTGGGGTATGGAAGTCATCTGTCCC  
TTCACTGTTTAGAGCATGACACTCTCCCCCTCAACAGCCTCCTGAGAAGGAAAGGATCTGCC  
CTGACCACTCCCCCTGGCACTGTTACTTGCCTCTGCGCCTCAGGGGTCCCCCTTCTGCACCGCT  
GGCTTCCACTCCAAGAAGGTGGACCAGGGTCTGCAAGTTCAACGGTCATAGCTGTCCCTCCA  
GGCCCCAACCTTGCCTCACCCTCCCGGCCCTAGTCTCTGCACCTCCTTAGGCCCTGCCTCT  
GGGCTCAGACCCCAACCTAGTCAAGGGGATTCTCCTGCTCTTAACTCGATGACTTGGGGCTC  
CCTGCTCTCCCGAGGAAGATGCTCTGCAGGAAAATAAAAGTCAGCCTTTTTCTAAAAAAA

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FIGURE 135

MAPALLLIPAA LASFILAFGTGVEFVRFTSLRPLLGGIPESGGPDARQGWLAALQDRSILAP  
LAWDLGLLLLFVGQHS LMAAERVKAWTSRYFGVLQRS LYVACTALALQLVMRYWEP I PKGPV  
LWEARAEPWATWVPLL CFVLHVISWLLIFSILLVFDYAELMGLKQVYYHVLGLGEPLALKSP  
RALRLFSHLRHPVCVELLTVLWVPTLGTDRLLLAFLLTLYLGLAHGLDQQDLRYLRAQLQR  
KLHLLSRPQDGEAE

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FIGURE 136

CCGAGCACAGGAGATTGCCTGCGTTTAGGAGGTGGCTGCGTTGTGGGAAAAGCTATCAAGGA  
AGAAATTGCCAAACCATGTCTTTTTTCTGTTTT CAGAGTAGTTCACAACAGATCTGAGTGT  
TTTAATTAAGCATGGAATACAGAAAAACAACAAAAA CTTAAGCTTTAATTT CATCTGGAATT  
CCACAGTTTTCTTAGCTCCCTGGACCCGGTTGACCTGTTGGCTCTTCCGCTGGCTGCTCTA  
TCACGTGGTGCTCTCCGACTACTACCCCGAGTGTAAGAACCTTCGGCTCGCGTGCTTCTG  
AGCTGCTGTGGATGGCCTCGGCTCTCTGGACTGTCTTCCGAGTAGGATGTCAC TGAGATCC  
CTCAAATGGAGCCTCCTGCTGCTGTCACTCCTGAGTTTCTTTGTGATGTGGTACCTCAGCCT  
TCCCCACTACAATGTGATAGAACGCGTGAAC TGGATGTACTTCTATGAGTATGAGCCGATT  
ACAGACAAGACTTTCACTTCACACTTCGAGAGCATTCAA CTGCTCTCATCAAAATCCATT  
CTGGTCATTCTGGTGACCTCCACCCCTTCAGATGTGAAAGCCAGGCAGGCCATTAGAGTTAC  
TTGGGGTGAAAAAAGTCTTGGTGGGGATATGAGGTTCTTACATTTTTCTTATTAGGCCAAG  
AGGCTGAAAAGGAAGACAAAATGTTGGCATTGTCCCTTAGAGGATGAACACCTTCTTTATGGT  
GACATAATCCGACAAGATTTTTTAGACACATATAATAACCTGACCTTGAAAACCATTTATGGC  
ATT CAGGTGGGTAAC TGAGTTTTGCCCAATGCCAAGTACGTAATGAAGACAGACACTGATG  
TTTTCATCAATACTGGCAATTTAGTGAAGTATCTTTTAAACCTAAACCACTCAGAGAAGTTT  
TTCACAGGTTATCCTCTAATTGATAATTATTCCTATAGAGGATTTTACCAAAAAACCCATAT  
TTCTTACCAGGAGTATCCTTTCAAGGTGTTCCCTCCATACTGCAGTGGGTGGGTTATATAA  
TGTC CAGAGATTTGGTGCCAAGGATCTATGAAATGATGGGT CACGTAAAACCCATCAAGTTT  
GAAGATGTTTATGTCTGGGATCTGTTTGAATTTATTAAGTGAACATT CATATTCAGAAGA  
CACAAATCTTTTCTTTCTATATAGAATCCATT TGGATGTCTGTCAACTGAGACGTGTGATTG  
CAGCCCATGGCTTTTCTTCCAAGGAGATCATCACTTTT TGGCAGGTCATGCTAAGGAACACC  
ACATGCCATTATTAACCTTCACATTCTACAAAAAGCCTAG AAGGACAGGATACCTTGTGGAAA  
GTGTTAAATAAAGTAGGTACTGTGGAAAATTCATGGGGAGGTCAGTGTGCTGGCTTACACTG  
AACTGAAACTCATGAAAAACCCAGACTGGAGACTGGAGGGTTACACTTGTGATTTATTAGTC  
AGGCCCTTCAAAGATGATATGTGGAGGAATTAAATATAAAGGAATTGGAGGTTTTTGTCTAAA  
GAAATTAATAGGACCAAACAATTTGGACATGTCACTTCTGTAGACTAGAAATTTCTTAAAAGGG  
TGTTACTGAGTTATAAGCTCACTAGGCTGTAAAAACAAA CAATGTAGAGTTTTTATTATTG  
AACAAATGTAGTCACTTGAAGGTTTTGTGTATATCTTATGTGGATTACCAATTTAAAAATATA  
TG TAGTTCTGTGTCAAAAACTTCTTCACTGAAGTTATACTGAACAAAATTTTACCTGTTTT  
TGGTCATTTTATAAAGTACTTCAAGATGTTGCAGTATTT CACAGTTATTATTATTTAAAATTA  
CTTCAACTTTTGTGTTTTTAAATGTTTTTGACGATTTCAATACAAGATAAAAAAGGATAGTGAAT  
CATTCTTTACATGCAAACATTTTCCAGTTACTTAACTGATCAGTTTATTATTGATACATCAC  
TCCATTAATGTAAAGTCATAGGTCATTATTGCATATCAGTAATCTCTTGGACTTTGTTAAAT  
ATTTTACTGTGGTAATATAGAGAAGAATTAAAGCAAGAAAATCTGAAA

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FIGURE 137

MASALWTVLP SRMSLRSLKWSLLLLSLLSFFVMWYLSLPHYNVIERVNW MYFYEYEP IYRQD  
FHFTLR:EH SNCSHQ NPFLVILVTSH PSDVKARQAIRVTWGEKKSWWGYEVLTFLLGQEA EK  
EDKMLALSLEDEHLLYGD IIRQDFLD TYNNLT LKTIMAFRWVTEFCPNAKYVMKTD TDVF IN  
TGNLVKYLLNLNHSEKFFTGYPLIDNYSYRGFYQKTHISYQEY PFKVFPPYCSGLGYIMSRD  
LVPRIYEMMGHV KPIKFEDVYVGICLNLLKVNIHIPEDTNLFFLYRIHLDVCQLRRVIAAHG  
FSSKEIITFWQVMLRN TTTCHY

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FIGURE 138

CCTCTGTCCACTGCTTTTCGTGAAGACAAGATGAAGTTCACAATTGTCTTTGCTGGACTTCTT  
GGAGTCTTTCTAGCTCCTGCCCTAGCTAACTATAATATCAACGTCAATGATGACAACAACAA  
TGCTGGAAGTGGGCAGCAGTCAGTGAGTGTCAACAATGAACACAATGTGGCCAATGTTGACA  
ATAACAACGGATGGGACTCCTGGAATTCCATCTGGGATTATGGAAATGGCTTTGCTGCAACC  
AGACTCTTTCAAAGAAGACATGCATTGTGCACAAAATGAACAAGGAAGTCATGCCCTCCAT  
TCAATCCCTTGATGCACTGGTCAAGGAAAAGAAGCTTCAGGGTAAGGGACCAGGAGGACCAC  
CTCCCAAGGGCCTGATGTACTCAGTCAACCCAAACAAAGTCGATGACCTGAGCAAGTTCGGA  
AAAAACATTGCAAACATGTGTCTGTGGGATTCCAACATACATGGCTGAGGAGATGCAAGAGGC  
AAGCCTGTTTTTTTACTCAGGAACGTGCTACACGACCAGTGTACTATGGATTGTGGACATTT  
CCTTCTGTGGAGACACGGTGGAGAACTAAACAATTTTTTAAAGCCACTATGGATTTAGTCAT  
CTGAATATGCTGTGCAGAAAAAATATGGGCTCCAGTGGTTTTTACCATGTCATTCTGAAATT  
TTTCTCTACTAGTTATGTTTGATTTCTTTAAGTTTCAATAAAATCATTTAGCATTGAAAAAAA

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FIGURE 139

MKFTIVFAGLLGVFLAPALANYNINVNDNNNAGSGQQSVSVNNEHNVANVDNNNGWDSWNS  
IWDYGNGFAATRLFQKKTCIVHKMNKEVMPSIQSLDALVKEKKLQGKGPGGPPPKGLMYSVN  
PNKVDDLKFGKNIANMCRGIPTYMAEEMQEASLFFYSGTCYTTSVLWIVDISFCGDTVEN

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FIGURE 140

CATTTCTGAAACTAATCGTGTGAGAATTGACTTTGAAAAGCATTGCTTTTTACAGAAGTATA  
TTAACTTTTTAGGAGTAATTTCTAGTTTGGATTGTAATATGAAATAATTTAAAAGGGCTTCG  
CTCATATATAGGAAAATCGCATATGGTCCTAGTATTAAATCTTATTGCTTACTGATTTTTT  
TGAGTTAAGAGTTGTTATATGCTAGAAATATGAGGATGTGAATATAAATAAGAGAAGAAAAA  
GAATAAAGTAGATTGAGTCTCCAATTTTATGTAAGCTTCAGAAGAACTGGTTTGTGTACATG  
CAAGCTTATAGTTGAAATATTTTTTCAGGAATTACATGAATGACAGTCTTCGAACCAATGTGT  
TTGTTTCGATTTCAACCAGAGACTATAGCATGTGCTTGCATCTACCTTGCAGCTAGAGCACTT  
CAGATTCGGTTGCCAACTCGTCCCCATTGGTTTTCTTCTTTTTGGTACTACAGAAGAGGAAAT  
CCAGGAAATCTGCATAGAAACACTTAGGCTTTATACCAGAAAAAGCCAACTATGAATTAC  
TGGAAAAAGAAGTAGAAAAAAGAAAAGTAGCCTTACAAGAAGCCAAATTTAAAGCAAAGGGA  
TTGAATCCGGATGGAACCTCAGCCCTTTCAACCCTGGGTGGATTTTCTCCAGCCTCCAAGCC  
ATCATCACCAGAGAAGTAAAAGCTGAAGAGAAATCACCAATCTCCATTAATGTGAAGACAG  
TCAAAAAAGAACCTGAGGATAGACAACAGGCTTCCAAAAGCCCTTACAATGGTGTAAGAAAA  
GACAGCAAGAGAAGTAGAAATAGCAGAAGTGCAAGTCGATCGAGGTCAAGAACACGATCAGG  
TTCTAGATCACATACTCCAAGAAGACACTATAATAATAGGCGGAGTCGATCTGGAACATACA  
GCTCGAGATCAAGAAGCAGGTCCCGCAGTCACAGTGAAAGCCCTCGAAGACATCATAATCAT  
GGTTCTCCTCACCTTAAGGCCAAGCATACCAGAGATGATTTAAAAAGTTCAAACAGACATGG  
TCATAAAAGGAAAAAATCTCGTTCTCGATCTCAGAGCAAGTCTCGGGATCACTCAGATGCAG  
CCAAGAAACACAGGCATGAAAGGGGACATCATAGGGACAGGCGTGAACGATCTCGCTCCTTT  
GAGAGGTCCCATAAAAGCAAGCACCATGGTGGCAGTCGCTCAGGACATGGCAGGCACAGGCG  
CTGA~~CT~~TTTTCTTTCCTTTGAGCCTGCATCAGTTCTTGGTTTTGCCTATCTACAGTGTGATGT  
ATGGACTCAATCAAAAACATTAAACGCAAACCTGATTAGGATTTGATTTCTTGAAACCCCTCTA  
GGTCTCTAGAACACTGAGGACAGTTTCTTTTGAAAAGAACTATGTTAATTTTTTGCACATT  
AAAATGCCCTAGCAGTATCTAATTAAAAACCATGGTCAGGTTCAATTGTACTTTATTATAGT  
TGTGTATTGTTTATTGCTATAAGAACTGGAGCGTGAATTCTGTAAAAATGTATCTTATTTTT  
ATACAGATAAAATTGCAGACACTGTTCTATTTAAGTGGTTATTTGTTTAAATGATGGTGAAT  
ACTTTCTTAACACTGGTTTGTCTGCATGTGTAAAGATTTTACAAGGAAATAAAATACAAAT  
CTTGTTTTTTCTAAAAAAGAAAAAAGT



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FIGURE 141

MNDSLRTNVFVRFQPETIACACIYLAARALQIPLPTRPHWFLFLFGTTEEEIQEICIETLRLY  
TRKKPNYELLEKEVEKRKVALQEAKLKAKGLNPDGTPALSTLGGFSFASKPSSPREVKAEEK  
SPISINVKTVKKEPEDRQQASKSPYNGVRKDSKRSRNSRSASRSRSRTRSRSRSHTPRRHYN  
NRRSRSGTYSSRSRSHSESPRRHHNHGSPHLKAKHTRDDLKSSNRHGHRKRSRSRSQ  
SKSRDHSDAAKKHRHERGHRDRRERSRSFERSHKSKHHGGSRSRSGHGRHRR

FIGURE 142

TGGGGATAAAGGAAAAATGGTCAGGTATTAATGGCTTAAAGATTATTGGAAGGGGTTTATCA  
TTTTTTGAANNTATTTCGGGTCANAATTGNCTTTGAAAAGCATTGCTTTTTACAGAAATATAT  
TANCTTTTTAGAGTAATTTCTAGTTTGGATTGTAATATGAAATTATTTAAAAGGGCTTCGCT  
CATATATAGGAAAATCGCATATGGTCCTAGTATTAAATTNTTATTGCTTACTGATTTTTTTG  
AGTTAAGAGTTGTTATATGNTAGAATATGAGGATGTGAATATAAATAAGAGAAGAAAAAAGA  
ATAAAGTAGATTGAGTCTCCAATTTTATGTAAGCTTCAGAAGAAGCTGGTTTGTTTACATGCA  
AGCTTATAGTTGAAATATTTTTCAGGAATTACATGAATGACAGTCTTCGAACCAATGTGTTT  
GTTTCGATTTCAACCAGAGANTATAGCATGTGCTTGCATCTACCTTGCAGNTAGAGCACTTCA  
GATTCCGTTGCCAACTNGTCCCCATTGGTTTCTTCTTTTGGTACTACAGAAGAGGAAATCC  
AGGAAATNTGCATAGAAACACTTAGGCTTTATACCAGAAAAAAGCCAAACTATGAATTACTG  
GAAAAAGAAGTAGAAAAAAGAAAAGTAGCCTTACAAGAAGCCNAATTAAAAGCAAAGGGATT  
GAATCCGGATGGAACTCCAGCCCTTTCAACCCTGGGTGGATTTTCTCC

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FIGURE 143

GGCACGAGGCCTCGTGCCAAGCTTGGCACGAGGGTGACCGCGTTCTCGCACGCGTCAATGGC  
GGTCCTCGGAGTACAGCTGGTGGTGACCCTGCTCACTGCCACCCTCATGCACAGGCTGGCGC  
CACACTGCTCCTTCGCGCGCTGGCTGCTCTGTAACGGCAGTTTGTTCGGATACAAGCACCCG  
TCTGAGGAGGAGCTTCGGGCCCTGGCGGGGAAGCCGAGGCCAGAGGCAGGAAAGAGCGGTG  
GGCCAATGGCCTTAGTGAGGAGAAGCCACTGTCTGTGCCCCGAGATGCCCCGTTCCAGCTGG  
AGACCTGCCCCCTCACGACCGTGATGCCCTGGTCTGCGCTTCTTCCTGGAGTACCAGTGG  
TTTGTGGACTTTGCTGTGTACTCGGGCGGCGTGACCTCTTCACAGAGGCCTACTACTACAT  
GCTGGGACCAGCCAAGGAGACTAACATTGCTGTGTTCTGGTGCCCTGCTCACGGTGACCTTCT  
CCATCAAGATGTTCCCTGACAGTGACACGGCTGTACTTCAGCGCCGAGGAGGGGGGTGAGCGC  
TCTGTCTGCCCTCACCTTTGCCCTTCCTCTTCCTGCTGCTGGCCATGCTGGTGCAAGTGGTGCG  
GGAGGAGACCCTCGAGCTGGGCCTGGAGCCTGGTCTGGCCAGCATGACCCAGAACTTAGAGC  
CACTTCTGAAGAAGCAGGGCTGGGACTGGGCGCTTCCTGTGGCCAAGCTGGCTATCCGCGTG  
GGACTGGCAGTGGTGGGCTCTGTGCTGGGTGCCTTCCTCACCTTCCCAGGCCTGCGGCTGGC  
CCAGACCCACCGGGACGCACTGACCATGTGCGAGGACAGACCCATGCTGCAGTTCCTCCTGC  
ACACCAGCTTCCTGTCTCCCCTGTTTCATCCTGTGGCTCTGGACAAAGCCCATTGCACGGGAC  
TTCTGCAACCAGCCCGCTTTGGGGAGACGCGTTTCTCCCTGCTGTCCGATTCTGCCTTCGA  
CTCTGGGCGCCTCTGGTTGCTGGTGGTGCTGTGCCTGCTGCGGCTGGCGGTGACCCGGCCCC  
ACCTGCAGGCCTACCTGTGCCTGGCCAAGGCCCGGGTGGAGCAGCTGCGAAGGGAGGCTGGC  
CGCATCGAAGCCCGTGAAATCCAGCAGAGGGTGGTCCGAGTCTACTGCTATGTGACCGTGGT  
GAGCTTGCAGTACCTGACGCCGCTCATCCTCACCCCTCAACTGCACACTTCTGCTCAAGACGC  
TGGGAGGCTATTCTGGGGCCTGGGCCCAGCTCCTCTACTATCCCCGACCCATCCTCAGCC  
AGCGCTGCCCCCATCGGCTCTGGGGAGGACGAAGTCCAGCAGACTGCAGCGCGGATTGCCGG  
GGCCTGGGTGGCCTGCTTACTCCCCTCTTCCTCCGTGGCGTCTGGCCTACCTCATCTGGT  
GGACGGCTGCCTGCCAGCTGCTCGCCAGCCTTTTCGGCCTCTACTTCCACCAGCACTTGGCA  
GGCTCCTAGCTGCCTGCAGACCCTCCTGGGGCCCTGAGGTCTGTTCTGGGGCAGCGGGACA  
CTAGCCTGCCCCCTCTGTTTGCGCCCCCGTGTCCCCAGCTGCAAGGTGGGGCCGGACTCCCC  
GGCGTTCCCTTCACCACAGTGCTGACCCGCGGCCCCCCTTGGACGCCGAGTTTCTGCCTCA  
GAACTGTCTCTCCTGGGCCCAGCAGCATGAGGGTCCCGAGGCCATTGTCTCCGAAGCGTATG  
TGCCAGGTTTGAGTGGCGAGGGTGATGCTGGCTGCTCTTCTGAACAAATAAAGGAGCATGCC  
GATTTTAA

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FIGURE 144

MAVLGVQLVVTLLTATLMHRLAPHCSFARWLLCNGSLFRYKHPSEEELRALAGKPRPRGRKE  
RWANGLSEEKPLSVPRDAPFQLETCPLTTVDALVLRFFLEYQWFVDFAVYSGGVYLFTEAYY  
YMLGPAKETNIAVFWCLLTVTFSIKMFLT VTRLYFSAEEGGERSVCLTFAFLFLLLAMLVQV  
VREETLELGLPGLASMTQNLEPLLKKQGWDWALPVAKLAIRVGLAVVGSVLGAFLTFPGLR  
LAQTHRDALTMSEDRPMLQFLLHTSFLSPLFILWLWTKPIARDFLHQPPFGETRFSLLSDSA  
FDSGRLWLLVVLCLLR LAVTRPHLQAYLCLAKARVEQLRREAGRIEAREIQQRVVRVYCYVT  
VVS LQYLTP LILTLNCTLLKTLGGYSWGLGPAPLLSPDPSSASAAPIGSGEDEVQQTAAARI  
AGALGGLLTPLFLRGVLAYLIWWTAAACQLLASLFGLYFHQHLA GS

FIGURE 145

CGTTNGCACGCGTCAATGGCGGTCTCGGAGTACAGCTGGTGGTGACCCTGCTCACTGCCAC  
CCTCATGCACAGGCTGGCGCCACACTGCTCCTTCGCGCGCTGGCTGCTCTGTAACGGCAGTT  
TGTTCCGATACAAGCACCCGNTTGTAGGAGGAGCTTCGGGCCCTGGCGGGGAAGCCGAGGCC  
CAGAGGCAGGAAAGAGCGGTGGGCCAATGGCCTTAGTGAGGAGAAGCCACTGTCTGTGCCCC  
GAGATGCCCCGTTCCAGCTGGAGACCTGCCCCCTCACGACCGTGGATGCCCTGGTCCTGCGC  
TTCTTCCTGGAGTACCAGTGGTTTGTGGACTTTGCTGTGTACTCGGGCGGCGGTACCTCTT  
CACAGAGGCCTACTACTACATGCTGGGACCAGCCAAGGAGACTAACATTGCTGTGTTCTGGT  
GCCTGCTCACAGTGACCTTCTCCATCAAGATGTTCTGACAGTGACACGGCTGTACTTCAGC  
GCCGAGGAGGGGGGTGAGCGCTCTGTCTGCCTCACCTTTGCCTTCCTCTTCCTGCTGCTGGC  
CATGCTGGTGCAAGCG

FIGURE 146

GGTTCCTACATCCTCTCATCTGAGAATCAGAGAGCATAATCTTCTTACGGGGCCCGTGATTTA  
TTAACGTGGCTTAATCTGAAGGTTCTCAGTCAAATCTTTGTGATCTACTGATTGTGGGGGC  
ATGGCAAGGTTTTCCTTAAAGGAGCTTGGCTGGTTTGGGGCCCTTGTTAGCTGACAGAAGGTGGC  
CAGGGAGAATGCAGCACACTGCTCGGAGAAATGAAGGCGCTTCTGTTGCTGGTCTTGCCCTTGG  
CTCAGTCCCTGCTAACTACATTGACAAATGTGGGCAACCTGCACTTCCTGTATTAGAACTCTG  
TAAAGGTGCCCTCCCCTACGGCCTGACCAAAGATAGGAAGAGGCGCTCACAAGATGGCTGTC  
CAGACGGCTGTGCGAGCCTCACAGCCACGGCTCCCTCCCAGAGGTTTCTGCAGCTGCCACC  
ATCTCCTTAATGACAGACGAGCCTGGCCTAGACAACCCTGCCTACGTGTCTCGGCAGAGGA  
CGGGCAGCCAGCAATCAGCCCAGTGGACTCTGGCCGGAGCAACCGAACTAGGGCACGGCCCT  
TTGAGAGTCCACTATTAGAAGCAGATCATTAAAAAAATAAATCGAGCTTTGAGTGTCTTT  
CGAAGGACAAAAGAGCGGGAGTGCAGTTGCCAACCATGCCGACCAGGGCAGGGAAAATTCTGA  
AAACACCCTAGCCCCCTGAAGTCTTTCCAAGGTTGTACCACCTGATTCCAGATGGTGAAATTA  
CCAGCATCAAGATCAATCGAGTAGATCCCAGTGAAAGCCTCTCTATTAGGCTGGTGGGAGGT  
AGCGAAACCCCACTGGTCCATATCATTATCCAACACATTTATCGTGATGGGGTGATCGCCAG  
AGACGGCCGGCTACTGCCAGGAGACATCATTCTAAAGGTCAACGGGATGGACATCAGCAATG  
TCCCTCACAACACGCTGTGCGTCTCCTGCGGCAGCCCTGCCAGGTGCTGTGGCTGACTGTG  
ATGCGTGAACAGAAGTTCCGCAGCAGGAACAAATGGACAGGCCCCGGATGCCACAGACCCCG  
AGATGACAGCTTTTCTGTGATTCTCAACAAAAGTAGCCCCGAGGAGCAGCTTGGAAATAAAC  
TGGTGCAGCAAGGTGGATGAGCCTGGGGTTTTTCATCTTCAATGTGCTGGATGGCGGTGTGGCA  
TATCGACATGGTCAGCTTGAGGAGAATGACCGTGTGTTAGCCATCAATGGACATGATCTTCG  
ATATGGCAGCCCAGAAAGTTCGGGCTCATCTGATTTCAGGCCAGTGAAAGACGTGTTACCTCG  
TCGTGTCCCCCAGGTTCCGGCAGCGGAGCCCTGACATCTTTCAGGAAGCCGGCTGGAACAGC  
AATGGCAGCTGGTCCCCAGGGCCAGGGGAGAGGAGCAACACTCCCAAGCCCCCTCCATCCTAC  
AATTACTTGTCTATGAGAAGGTGGTAAATATCCAAAAGACCCCGGTGAATCTCTCGGCATGA  
CCGTGCGAGGGGGAGCATCACATAGAGAATGGGATTTGCCTATCTATGTCATCAGTGTGAG  
CCCGGAGGAGTCATAAGCAGAGATGGAAGAATAAAAAAGGTGACATTTTGTGTAATGTGGA  
TGGGGTCGAACTGACAGAGGTGAGCCGGAGTGAGGCAGTGGCATTATTGAAAAGAACATCAT  
CCTCGATAGTACTCAAAGCTTTGGAAGTCAAAGAGTATGAGCCCCAGGAAGACTGCAGCAGC  
CCAGCAGCCCTGGACTCCAACCACAACATGGCCCCACCCAGTGACTGGTCCCCATCCTGGGT  
CATGTGGCTGGAATTACCACGGTGCTTGTATACTGTAAAGATATTGTATTACGAAGAAACA  
CAGCTGGAAGTCTGGGCTTCTGCATTGTAGGAGGTTATGAAGAATACAATGGAAACAAACCT  
TTTTTTCATCAAATCCATTGTTGAAGGAACACCAGCATACAATGATGGAAGAATTAGATGTGG  
TGATATTCTTCTGTCTCAATGGTAGAAGTACATCAGGAATGATACATGCTTGCTTGGCAA  
GACTGCTGAAAGAACTTAAAGGAAGAATTACTCTAACTATTGTTTCTTGGCCTGGCACTTTT  
TTATAAATCAATGATGGGTGAGGAAAACAGAAAAATCACAAATAGGCTAAGAAGTTGAA  
ACACTATATTTATCTTGTGAGTTTTTATATTTAAAGAAAGAAATACATTGTAAAAATGTCAGG  
AAAAGTATGATCATCTAATGAAAGCCAGTTACACCTCAGAAAATATGATTCCAAAAAATTA  
AACTACTAGTTTTTTTTTTCAGTGTGGAGGATTTCTCATTACTCTACAACATTGTTTATATTT  
TTTCTATTCAATAAAAAGCCCTAAAACAATAAATGATTGATTGTATACCCCACTGAATT  
CAAGCTGATTTAAATTTAAATTTGGTATATGCTGAAGTCTGCCAAGGGTACATTATGGCCA  
TTTTTAATTTACAGCTAAAATATTTTTTAAATGCATTGCTGAGAAACGTTGCTTTTCATCAA  
ACAAGAATAAATATTTTTTCAGAAGTTAAA

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FIGURE 147

MKALLLLVLPWLSPANYIDNVGNLHFLYSELCKGASHYGLTKDRKRRSQDGC PDGCASLTAT  
APSPEVSAAATISLMTDEPGLDNPAYVSSAEDGQPAISPVD SGRSNRTRARPFERSTIRSRS  
FKKINRALSVLRRTKSGSAVANHADQGRESENTTAPEVFPRLYHLIPDGEITSIKINRVDP  
SESLSIRLVGGSETPLVHII IQHIYRDGVIARDGRLLPGDIILKVNGMDISNVPHNYAVRLL  
RQPCQVLWLTVMREQKFRSRNNGQAPDAYRPRDDSFHVILNKSSPEEQLG IKLVRKVDEPGV  
FIFNVLDGGVAYRHGQLEENDRVLAINGHDLRYGSPESA AHLIQASERRVHLVVSQRQVRQRS  
PDIFQEAGWNSNGSWSPGPGERSNTPKPLHPTITCHEKV VNIQKDPGESLGMTVAGGASHRE  
WDLPIYVISVEPGGVISRDGRIKTDILLNVDGVELTEVSRSEAVALLKRTSSSIVLKALEV  
KEYEPQEDCSSPAALDSNHNMAPPSDWSPSWVMWLELPRCLYNCKDIVLRRNTAGSLGFCIV  
GGYEEYNGNKPF FIKSIVEGTPAYNDGRIRCGDILLAVNGRSTSGMIHACLARLLKELKGRI  
TLTIVSWPGTFL

FIGURE 148

CCAAAGTGATCATTTGAAAAAGAGATATCCACATCTTCAAGCCCATATAAAGGATAGAAGCT  
GCACAGGGCAGCTTTACTTACTCCAGCACCTTCCTCTCCCAGGCAAATGGTGCTGACCATCT  
TTGGGATACAATCTCATGGATACGAGGTTTTTAACATCATCAGCCCAAGCAACAATGGTGGC  
AATG TTCAGGAGACAGTGACAATTGATAATGAAAAAATACCGCCATCGTTAACATCCATGC  
AGGATCATGCTCTTCTACCACAATTTTTGACTATAAACATGGCTACATTGCATCCAGGGTGC  
TCTCCCGAAGAGCCTGCTTTATCCTGAAGATGGACCATCAGAACATCCCTCCTCTGAACAAT  
CTCCAATGGTACATCTATGAGAAACAGGCTCTGGACAACATGTTCTCCAACAAATACACCTG  
GGTCAAGTACAACCCTCTGGAGTCTCTGATCAAAGACGTGGATTGGTTCCTGCTTGGGTCAC  
CCATTGAGAACTCTGCAAACATATCCCTTTGTATAAGGGGGAAGTGGTTGAAAACACACAT  
AATGTCGGTGCTGGAGGCTGTGCAAAGGCTGGGCTCCTGGGCATCTTGGGAATTTCAATCTG  
TGCAGACATTATGTTTAGGATGATTAGCCCTCTTGTTTTATCTTTTCAAAGAAATACATCC  
TTGGTTTACACTCAAAGTCAAATTAAATTCTTTCCCAATGCCCCAACTAATTTTGAGATTC  
AGTCAGAAAATATAAATGCTGTATTTATA



FIGURE 149

MKILVAFLVVLTFGIQSHGYEVFNIIISPSNNGGNVQETVTIDNEKNTAIVNIHAGSCSSTT  
IFDYKHGYIASRVLSRRACFILKMDHQNIPLNNLQWYIYEKQALDNMFSENKYTWVKYNPLE  
SLIKDVDWFLLGSPIEKLCKHIPLYKGEVVENTHNVGAGGCAKAGLLGILGISICADIHV

FIGURE 150

GGCACGAGCCAGGAAGTAGGAGGTTCTCACTGCCCCGAGCAGAGGCCCTACACCCACCGAGGC  
ATGGGGCTCCCTGGGCTGTTCTGCTTGGCCGTGCTGGCTGCCAGCAGCTTCTCCAAGGCACG  
GGAGGAAGAAATTACCCCTGTGGTCTCCATTGCCTACAAAGTCCTGGAAGTTTTCCCCAAAG  
GCCGCTGGGTGCTCATAACCTGCTGTGCACCCAGCCACCACCGCCCATCACCTATTCCCTC  
TGTGGAACCAAGAACATCAAGGTGGCCAAGAAGGTGGTGAAGACCCACGAGCCGGCCTCCTT  
CAACCTCAACGTCACTCAAGTCCAGTCCAGACCTGCTCACCTACTTCTGCCGGGCGTCCT  
CCACCTCAGGTGCCCATGTGGACAGTGCCAGGCTACAGATGCACTGGGAGCTGTGGTCCAAG  
CCAGTGTCTGAGCTGCGGGCCAACTTCACTCTGCAGGACAGAGGGGCAGGCCCCAGGGTGGA  
GATGATCTGCCAGGCGTCCTCGGGCAGCCACCTATCACCAACAGCCTGATCGGGAAGGATG  
GGCAGGTCCACCTGCAGCAGAGACCATGCCACAGGCAGCCTGCCAACTTCTCCTTCCTGCCG  
AGCCAGACATCGGACTGGTTCTGGTGCCAGGCTGCAAACAACGCCAATGTCCAGCACAGCGC  
CCTCACAGTGGTGCCCCCAGGTGGTGACCAGAAGATGGAGGACTGGCAGGGTCCCCTGGAGA  
GCCCCATCCTTGCCCTTGCCGCTCTACAGGAGCACCCGCCGTCTGAGTGAAGAGGAGTTTGGG  
GGGTTCAGGATAGGGAATGGGGAGGTGAGAGGACGCAAAGCAGCAGCCATGTAGAATGAACC  
GTCCAGAGAGCCAAGCACGGCAGAGGACTGCAGGCCATCAGCGTGCACTGTTTCGTATTGGA  
GTTTCATGCAAAATGAGTGTGTTTTAGCTGCTCTTGCCACAAAAAAAAAAAAAAAAAAAAA

FIGURE 151

MGLPGLFCLAVLAASSFSKAREEEITPVVSIAYKVLEVFPKGRWVLITCCAPQPPPPITYSL  
CGTKNIKVAKKVVKTHEPASFNLNVTLM<sup>1</sup>SSPDLLTYFCRASSTSGAHVDSARLQMHWELWSK  
PVSELNANFTLQDRGAGPRVEMICQASSGSPPITNSLIGKDGQVHLQQRPCHRQPANFSFLP  
SQTSDWFWCQAANNANVQHSALTVVPPGGDQKMEDWQGPLESPILALPLYRSTRRLSEEEFG  
GFRIGNGEVRGRKAAAM

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FIGURE 152

GGTCCTTAATGGCAGCAGCCGCCGTACCAAGATCCTTCTGTGCCTCCCGCTTCTGCTCCTG  
CTGTCCGGCTGGTCCCGGGCTGGGCGAGCCGACCCTCACTCTCTTTGCTATGACATCACCGT  
CATCCCTAAGTTCAGACCTGGACCACGGTGGTGTGCGGTTCAAGGCCAGGTGGATGAAAAGA  
CTTTTCTTCACTATGACTGTGGCAACAAGACAGTCAACCTGTCAGTCCCCTGGGGAAGAAA  
CTAAATGTCAACCGCCTGGAAAGCACAGAACCCAGTACTGAGAGAGGTGGTGGACATACT  
TACAGAGCAACTGCGTGACATTCACTGGAGAATTACACACCCAAGGAACCCCTCACCTGC  
AGGCAAGGATGTCTTGTGAGCAGAAAGCTGAAGGACACAGCAGTGGATCTTGGCAGTTCAGT  
TTCGATGGGCAGATCTTCCTCCTCTTTGACTCAGAGAAGAGAATGTGGACAACGGTTCATCC  
TGGAGCCAGAAAGATGAAAGAAAAGTGGGAGAATGACAAGGTTGTGGCCATGTCCTTCCATT  
ACTTCTCAATGGGAGACTGTATAGGATGGCTTGAGGACTTCTTGATGGGCATGGACAGCACC  
CTGGAGCCAAGTGCAGGAGCACCCTCGCCATGTCTCAGGCACAACCCAACTCAGGGCCAC  
AGCCACCACCCTCATCCTTTGCTGCCTCCTCATCATCCTCCCCTGCTTCATCCTCCCTGGCA  
TCTGAGGAGAGTCCTTTAGAGTGACAGGTTAAAGCTGATACCAAAAGGCTCCTGTGAGCAG  
GTCTTGATCAAACCTCGCCCTTCTGTCTGGCCAGCTGCCCACGACCTACGGTGTATGTCCAGT  
GGCCTCCAGCAGATCATGATGACATCATGGACCCAATAGCTCATTCACTGCCTTGATTCTTT  
TTGCCAACAAATTTTACCAGCAGTTATACCTAACATATTATGCAATTTTCTCTTGGTGTACC  
TGATGGAATTCTTGCACTTAAAGTTCTGGCTGACTAAACAAGATATATCATTTTCTTTCTTC  
TCTTTTTGTTTGGAAAATCAAGTACTTCTTTGAATGATGATCTCTTTCTTGCAAATGATATT  
GTCAGTAAAATAATCACGTTAGACTTCAGACCTCTGGGGATTCTTCCGTGTCCTGAAAGAG  
AATTTTTAAATTATTTAATAAGAAAAAATTTATATTAATGATTGTTTCCTTTAGTAATTTAT  
TGTTCTGTACTGATATTTAAATAAAGAGTTCTATTTCCCAAAAAAAAAAAAAAAAAAAAA

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FIGURE 153

MAAAAATKILLCLPLLLLLSGWSRAGRADPHSLCYDITVIPKFRPGPRWCAVQGQVDEKTFL  
HYDCGNKTVTPVSPPLGKKLNVTTAWKAQNPVLREVVDILTEQLRDIQLENYTPKEPLTLQAR  
MSCEQKAEGHSSGSWQFSFDGQIFLLFDSEKRMWTTVHPGARKMKEKWENDKVVAMSFHYFS  
MGDCIGWLEDFLMGMDSTLEPSAGAPLAMSSGTTQLRATATTLILCCLLIILPCFILPGI

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FIGURE 154

GGGAAAGCCATTTGCGAAAACCCATCTATACAACTATATATTTTCATTTCTGCTGCTAGCTG  
CCTTGGGCCTCACAATTTTCATTCTGTTTTCTGACTTTCAAGTTATATACCGTGGAAATGGAG  
TTGATCCCAACCATAACATCGTGGAGGGTTTTAATTTTGGTGGTAGCCCTCACCCAATTCTG  
GTGTGGCTTTCTTTGCAGAGGATTCCACCTTCAAAATCATGAACTCTGGCTGTTGATCAAAA  
GAGAATTTGGATTCTACTCTAAAAGTCAATATAGGACTTGGCAAAAGAAGCTAGCAGAAGAC  
TCAACCTGGCCTCCCATAAACAGGACAGATTATTCAGGTGATGGCAAAAATGGATTCTACAT  
CAACGGAGGCTATGAAAGCCATGAACAGATTCCAAAAAGAAAACCTCAAATTGGGAGGCCAAC  
CCACAGAACAGCATTCTGGGCCAGGCTGTAATCAGAATTGTCGTCGTACATGCTCAACAGC  
ATTGCTTTTTTCCCCAAAATTAACACATTGTGGAGAAGTGATGATACTCTCCCCTTACCTTT  
CCTCTCTCCATTCAAGCATTCAAAGTATATTTTCAATGAATTAAACCTTGCAGCAAGGGACC  
TTAGATAGGCTTATTCTGACTGTATGCTTTACCAATGAGAGAAAAAAATGCATTTCTGTAT  
CATCCTTTTCAATAAACTGTATTTCATTTTGAAAAAAAAAAAAAAAAAAAAA

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FIGURE 155

MELIPTITSWRVLILVVALTQFWCGFLCRGFHLQNHFWLLIKREFGFYSKSQYRTWQKKLA  
EDSTWPPINRTDYSGDGKNGFYINGGYESHEQIPKRKLKLGQPTQHFWARL

FIGURE 156

GTTCCTCTTCCGAGCCAAAATCCCAGGCGATGGTGAATTATGAACGTGCCACACCATGAAG  
CTCTTGTTGGCAGGTAACTGTGCACCACCACACCTGGAATGCCATCCTGCTCCCGTTCTGCTA  
CCTCACGGCGCAAGTGTGGATTCTGTGTGCAGCCATCGCTGCTGCCGCCTCAGCCGGGCCCC  
AGAACTGCCCCCTCCGTTTGTCTGTGCAGTAACCAGTTTCAGCAAGGTGGTGTGCACGCGCCGG  
GGCCTCTCCGAGGTCCCGCAGGGTATTCCCTCGAACACCCGGTACCTCAACCTCATGGAGAA  
CAACATCCAGATGATCCAGGCCGACACCTTCCGCCACCTCCACCACCTGGAGGTCTGCACT  
TGGGCAGGAACTCCATCCGGCAGATTGAGGTGGGGGCCCTTCAACGGCCTGGCCAGCCTCAAC  
ACCTTGGAGCTGTTTCGACAACTGGCTGACAGTCATCCCTAGCGGGGCCCTTTGAATACCTGTC  
CAAGCTGCGGGAGCTCTGGCTTCGCAACAACCCCATCGAAAGCATCCCCTCTTACGCCTTCA  
ACCGGGTGCCCTCCCTCATGCGCTGGACTTGGGGGAGCTCAAGAAGCTGGAGTATATCTCT  
GAGGGAGCTTTTGGGGGCTGTTCAACCTCAAGTATCTGAACTTGGGCATGTGCAACATTAA  
AGACATGCCCAATCTCACCCCCCTGGTGGGGCTGGAGGAGCTGGAGATGTGAGGGAACCACT  
TCCCTGAGATCAGGCCTGGCTCCTTCCATGGCCTGAGCTCCCTCAAGAAGCTCTGGGTATG  
AACTCACAGGTCAGCCTGATTGAGCGGAATGCTTTTTCGCGGGCTGGCTTCACTTGTGGAAC  
CAACTTGGCCCAATAACCTCTCTTCTTTGCCCCATGACCTCTTTACCCCGCTGAGGTACC  
TGGTGGAGTTGCATCTACACCACAACCTTGGAACTGTGATTGTGACATTCTGTGGCTAGCC  
TGGTGGCTTCGAGAGTATATACCCACCAATTCCACCTGCTGTGGCCGCTGTGATGCTCCCAT  
GCACATGCGAGGCCGCTACCTCGTGGAGGTGGACCAGGCCTCCTTCCAGTGCTCTGCCCCCT  
TCATCATGGACGCACCTCGAGACCTCAACATTTCTGAGGGTCGGATGGCAGAACTTAAGTGT  
CGGACTCCCCCTATGTCTCTCCGTGAAGTGGTTGCTGCCCAATGGGACAGTGCTCAGCCACGC  
CTCCCGCCACCCAAAGGATCTCTGTCTCTCAACGACGGCACCTTGAACCTTTTCCACGTGCTGC  
TTTCAGACACTGGGGTGTACACATGCATGGTGACCAATGTTGCAGGCAACTCCAACGCCTCG  
GCCTACCTCAATGTGAGCACGGCTGAGCTTAACACCTCCAACCTACAGCTTCTTACCACAGT  
AACAGTGGAGACCACGGAGATCTCGCCTGAGGACACAACGCGAAAGTACAAGCCTGTTCTTA  
CCACGTCCACTGGTTACCAGCCGGCATATACCACCTCTACCACGGTGCTCATTACAGACTACC  
CGTGTGCCCAAGCAGGTGGCAGTACCCGCGACAGACACCACTGACAAGATGCAGACCAGCCT  
GGATGAAGTCATGAAGACCACCAAGATCATCATTGGCTGCTTTGTGGCAGTGACTCTGCTAG  
CTGCCGCCATGTTGATTGTCTTCTATAAACTTCGTAAGCGGCACCAGCAGCGGAGTACAGTC  
ACAGCCGCCCGGACTGTTGAGATAATCCAGGTGGACGAAGACATCCAGCAGCAACATCCGC  
AGCAGCAACAGCAGCTCCGTCCGGTGTATCAGGTGAGGGGGCAGTAGTGCTGCCCACAATTC  
ATGACCATATTAACACACCTACAAACCAGCACATGGGGCCCACTGGACAGAAAAACAGC  
CTGGGGAACTCTCTGCACCCACAGTCACCACTATCTCTGAACCTTATATAATTAGACCCA  
TACCAAGGACAAGGTACAGGAACTCAAATATGACTCCCTCCCCCAAAAACTTATAAAAT  
GCAATAGAATGCACACAAAGACAGCAACTTTTGTACAGAGTGGGGAGAGACTTTTCTTGTA  
TATGCTTATATATTAAGTCTATGGGCTGGTTAAAAAAAACAGATTATATTAATAATTTAAAGA  
CAAAAAGTCAAAAACA



FIGURE 157

MKLLWQVTVHHHTWNAILLPFVYLTAQVWILCAAIAAAAASAGPQNCPSVCSCSNQFSKVVCT  
RRGLSEVPQGI PSNTRYLNLMENNIQMIQADTFRHLHHLEVLQLGRNSIRQIEVGAFNGLAS  
LNTLELFDNWLTVIPSGAFEYLSKLRELWLRNNPIESIPSYAFNRVPSLMRLDLGELKKLEY  
ISEGAFEGFLNLKYLNLGMCNIKDMPNLTPLVGLEELEMMSGNHFP EIRPGSFHGLSSLKKLW  
VMNSQVSLIERNAFDGLASLVELNLAHNNLSSLP HDLFTPLRYLVELHLHHPWNCD CDILW  
LAWWLREYIPTNSTCCGRCHAPMHMRGRYLVEVDQASFQCSAPFIMDAPRDLNISEGRMAEL  
KCRTPPMSSVKWLLPNGTVLSHASRHPRI SVLNDGTLNFSHVLLSDTGVYTCMVTNVAGNSN  
ASAYLNVSTAE LNTSNYSFFTTVTVETTEISPEDTTRKYKPVPTTSTGYQPAYTTSTTVLIQ  
TTRVPKQVAVPATD TTDKMQTS LDEVMKTTKIIIGCFVAVTLLAAAMLIVFYKLRKRHQQRS  
TVTAARTVEIIQVDEDIPAATSAAATAAPSGVSGEGAVVLPTIHDHINYNTYKPAHGAHWTE  
NSLGNLHPTVTTISEPYIIQHTKDKVQETQI

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FIGURE 158

CGCTCGGGCACCAGCCGCGGCAAGGATGAGCTGGGTTGCTGGACGCAGTTGGGGCTCACTT  
TTCTTCAGCTCCTTCTCATCTCGTCCCTTGCJAAGAGAGTACACAGTCATTAATGAAGCCTGC  
CCTGGAGCAGAGTGGAATATCATGTGTCGGGAGTGCTGTGAATATGATCAGATTGAGTGCGT  
CTGCCCCGGAAGAGGGGAAGTCGTGGGTATACCATCCCTTGCTGCAGGAATGAGGAGAATG  
AGTGTGACTCCTGCCTGATCCACCCAGGTTGTACCATCTTTGAAAACCTGCAAGAGCTGCCGA  
AATGGCTCATGGGGGGGTACCTTGATGACTTCTATGTGAAGGGGTTCTACTGTGCAGAGTG  
CCGAGCAGGCTGGTACGGAGGAGACTGCATGCGATGTGGCCAGGTTCTGCGAGCCCCAAAGG  
GTCAGATTTTGTGGAAAGCTATCCCCTAAATGCTCACTGTGAATGGACCATTATGCTAAA  
CCTGGGTTTGTCCAACTAAGATTTGTATGTTGAGTCTGGAGTTTGAATACATGTGCCA  
GTATGACTATGTTGAGGTTTCGTGATGGAGACAACCGCGATGGCCAGATCATCAAGCGTGTCT  
GTGGCAACGAGCGGCCAGCTCCTATCCAGAGCATAGGATCCTCACTCCACGTCCTCTTCCAC  
TCCGATGGCTCCAAGAATTTTGACGGTTTCCATGCCATTTATGAGGAGATCACAGCATGCTC  
CTCATCCCCTTGTTCATGACGGCACGTGCGTCTTGACAAGGCTGGATCTTACAAGTGTG  
CCTGCTTGGCAGGCTATACTGGGCAGCGCTGTGAAAATCTCCTTGAAGAAAGAACTGCTCA  
GACCCTGGGGGCCAGTCAATGGGTACCAGAAAATAACAGGGGGCCCTGGGCTTATCAACGG  
ACGCCATGCTAAAATTGGCACCGTGGTGTCTTTCTTTTGTAACTCCTATGTTCTTAGTG  
GCAATGAGAAAAGAACTTGCCAGCAGAATGGAGAGTGGTCAGGGAAACAGCCCATCTGCATA  
AAAGCCTGCCGAGAACCAGATTTTCAACCTGGTGAGAAGGAGAGTTCTTCCGATGCAGGT  
TCAGTCAAGGGAGACACCATTACACCAGCTATACTCAGCGGCCTTCAAGCAGAGAACTGC  
AGAGTGGCCCTACCAAGAAGCCAGCCCTTCCCTTTGGAGATCTGCCCATGGGATACCAACAT  
CTGCATACCCAGCTCCAGTATGAGTGCATCTCACCTTCTACCGCCGCTGGGCAGCAGCAG  
GAGGACATGTCTGAGGACTGGGAAGTGGAGTGGGCGGGCACCATCCTGCATCCCTATCTGCG  
GGAAAATTGAGAACATCACTGCTCCAAAGACCCAAGGGTTGCGCTGGCCGTGGCAGGCAGCC  
ATCTACAGGAGGACCAGCGGGGTGCATGACGGCAGCCTACACAAGGGAGCGTGGTTCTAGT  
CTGCAGCGGTGCCCTGGTGAATGAGCGCACTGTGGTGGTGGCTGCCCACTGTGTTACTGACC  
TGGGGAAGGTCAACATGATCAAGACAGCAGACCTGAAAGTTGTTTTGGGGAATTTCTACCGG  
GATGATGACCGGGATGAGAAGACCATCCAGAGCCTACAGATTTCTGCTATCATTCTGCATCC  
CAACTATGACCCCATCCTGCTTGATGCTGACATCGCCATCCTGAAGCTCCTAGACAAGGCC  
GTATCAGCACCCGAGTCCAGCCCATCTGCCTCGCTGCCAGTCGGGATCTCAGCACTTCTTTC  
CAGGAGTCCCACATCACTGTGGCTGGCTGGAATGTCTTGGCAGACGTGAGGAGCCCTGGCTT  
CAAGAACGACACACTGCGCTCTGGGGTGGTCACTGTGGTGGACTCGCTGCTGTGTGAGGAGC  
AGCATGAGGACCATGGCATCCCAGTGAGTGTCACTGATAACATGTTCTGTGCCAGCTGGGAA  
CCCACTGCCCCCTTCTGATATCTGCACTGCAGAGACAGGAGGCATCGCGGCTGTGTCTTCCC  
GGGACGAGCATCTCCTGAGCCACGCTGGCATCTGATGGGACTGGTCAGCTGGAGCTATGATA  
AAACATGCAGCCACAGGCTCTCCACTGCCTTACCAAGGTGCTGCCTTTTAAAGACTGGATT  
GAAAGAAATATGAAATGAACCATGCTCATGCACTCCTTGAGAAGTGTCTGTATATCCGTC  
TGTACGTGTGTCATTGCGTGAAGCAGTGTGGGCCTGAAGTGTGATTGGCCTGTGAACCTGG  
CTGTGCCAGGGCTTCTGACTTCAGGGACAAAACCTCAGTGAAGGGTGAGTAGACCTCCATTGC  
TGGTAGGCTGATGCCGCTCCACTACTAGGACAGCCAATTGGAAGATGCCAGGGCTTGCAAG  
AAGTAAGTTTCTTCAAAGAAGACCATATACAAAACCTCTCCACTCCACTGACCTGGTGGTCT  
TCCCCAACTTTTCAAGTTTCTAGAGAGCTGCCTGTGGGACAGCCAGGGCAGCAGAGC  
GCCCCTTTTGAGGCTCTCAAGTTCTAGAGAGCTGCCTGTGGGACAGCCAGGGCAGCAGAGC  
TGGGATGTGGTGCATGCCTTTGTGTACATGGCCACAGTACAGTCTGGTCTTTTCTTCCCC  
ATCTCTGTACACATTTTAAATAAAATAAGGGTTGGCTTCTGAACTACAAAAA  
AA  
AA

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FIGURE 159

MELGCWTQLGLTFLQLLLISSLPREYTVINEACPGAENIMCRECCEYDQIECVCPGKREV  
GYTIPCCRNEENECDSCLIHPGCTIFENCKSCRNGSWGGLDDFYVKGIFYCAECRAGWYGGI  
CMRCGQVLRAPKGQILLESYPLNAHCEWTIHAKPGFVIQLRFVMLSLEFDYMCQYDYVEVRD  
GDNRDGQIIKRVCGNERPAPIQSIGSSLHVLFHSDGSKNFDGFAIYEEITACSSSPCFHDG  
TCVLDKAGSYKACLAGYTGQRCENLLEERNCSDPGGPVNGYQKITGGPGLINGRHAKIGTV  
VSFFCNNSYVLSGNEKRTCQQNGEWSGKQPICIKACREPKISDLVRRRVLPQVQSRETPLH  
QLYSAAFSKQKLQSAPTKKPALPFGDLPMGYQHLHTQLQYECISPFYRRLGSSRRTCLRTGK  
WSGRAPSCIPICGKIENITAPKTQGLRWPWQAAIYRRTSGVHDGSLHKGAWFLVCSGALVNE  
RTVVVAHCVTDLGKVMTIKTADLKVVVLGKFYRDDDRDEKTIQSLQISAIILHPNYDPILLD  
ADIAILKLLDKARISTRVQPICLAASRDLSTSFQESHITVAGWNVLADVRSPGFKNDTLRSG  
VVSVDSSLCEEQHEDHGIPVSVTDNMFCASWEPTAPSDICTAETGGIAAVSFPGRASPEPR  
WHLMLVSWSYDKTCSHRLSTAFTKVLFPKDWIERNMK

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FIGURE 160

ACCAGGCATTGTATCTTCAGTTGTCATCAAGTTCGCAATCAGATTGGAAAAGCTCAACTTGA  
AGCTTTCTTGCCCTGCAGTGAAGCAGAGAGATAGATATTATTACGTAATAAAAAACATGGGC  
TTCAACCTGACTTTCCACCTTTCCTACAAATTCGATTACTGTTGCTGTTGACTTTGTGCCT  
GACAGTGGTTGGGTGGGCCACCAGTAACCTTCGTGGGTGCCATTCAAGAGATTCTCTAAAG  
CAAAGGAGTTTATGGCTAATTTCCATAAGACCCCTCATTTTGGGGAAGGGAAAACTCTGACT  
AATGAAGCATCCACGAAGAAGGTAGAACTTGACAACCTGTCCTTCTGTGTCTCCTTACCTCAG  
AGGCCAGAGCAAGCTCATTTTCAAACCAGATCTCACTTTGGAAGAGGTACAGGCAGAAAATC  
CCAAAGTGTCCAGAGGCCGGTATCGCCCTCAGGAATGTAAAGCTTTACAGAGGGTCGCCATCCTC  
GTTCCCCACCGGAACAGAGAGAAACACCTGATGTACCTGCTGGAACATCTGCATCCCTTCCT  
GCAGAGGCAGCAGCTGGATTATGGCATCTACGTATCCACCAGGCTGAAGGTAAAAAGTTTA  
ATCGAGCCAACTCTTGAATGTGGGCTATCTAGAAGCCCTCAAGGAAGAAAATTGGGACTGC  
TTTATATTCCACGATGTGGACCTGGTACCCGAGAATGACTTTAACCTTTACAAGTGTGAGGA  
GCATCCCAAGCATCTGGTGGTTGGCAGGAACAGCACTGGGTACAGGTTACGTTACAGTGGAT  
ATTTTGGGGGTGTTACTGCCCTAAGCAGAGAGCAGTTTTTCAAGGTGAATGGATTCTCTAAC  
AACTACTGGGGATGGGGAGGCGAAGACGATGACCTCAGACTCAGGGTTGAGCTCCAAAGAAT  
GAAAATTTCCCGCCCCCTGCCTGAAGTGGGTAAATATACAATGGTCTTCCACACTAGAGACA  
AAGGCAATGAGGTGAACGCAGAACGGATGAAGCTCTTACACCAAGTGTACAGAGTCTGGAGA  
ACAGATGGGTTGAGTAGTTGTTCTTATAAATTAGTATCTGTGGAACACAATCCTTTATATAT  
CAACATCACAGTGGATTTCTGGTTTGGTGCATGACCCTGGATCTTTTGGTGATGTTTGGAAAG  
AACTGATTCTTTGTTTGCAATAATTTTGGCCTAGAGACTTCAAATAGTAGCACACATTAAGA  
ACCTGTTACAGCTCATTGTTGAGCTGAATTTTTCTTTTTGTATTTTCTTAGCAGAGCTCCT  
GGTGATGTAGAGTATAAAACAGTTGTAACAAGACAGCTTTCTTAGTCATTTTGATCATGAGG  
GTTAAATATTGTAATATGGATACTTGAAGGACTTTATATAAAAGGATGACTCAAAGGATAAA  
ATGAACGCTATTTGAGGACTCTGGTTGAAGGAGATTTATTTAAATTGAAAGTAATATATTAT  
GGGATAAAAGGCCACAGGAAATAAGACTGCTGAATGTCTGAGAGAACCAGAGTTGTTCTCGT  
CCAAGGTAGAAAGGTACGAAGATACAATACTGTTATTATTTATCCTGTACAATCATCTGTG  
AAGTGGTGGTGTGAGGTGAGAAGGCGTCCACAAAAGAGGGGAGAAAAGGCGACGAATCAGGA  
CACAGTGAACCTTGGGAATGAAGAGGTAGCAGGAGGGTGGAGTGTGGCTGCAAAGGCAGCAG  
TAGCTGAGCTGGTTGCAGGTGCTGATAGCCTTCAGGGGAGGACCTGCCCAGGTATGCCTTCC  
AGTGATGCCCACCAGAGAATACATTCTCTATTAGTTTTTAAAGAGTTTTTGTAAAATGATTT  
TGTACAAGTAGGATATGAATTAGCAGTTTACAAGTTTACATATTAATAATAATAATATGT  
CTATCAAATACCTCTGTAGTAAATGTGAAAAGCAAAA

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FIGURE 161

MGFNLTfHLSYKFRLLLLLTLCITVVGWATSNYFVGAIQEIPKAKEFMANFHKTLLLGKGKT  
LTNEASTKKVELDNCPSVSPYLRGQSKLIFKPDLTLEEVQAENPKVSRGRYRPQECKALQRV  
AILVPHRNREKHLMYLLEHLHPFLQRQQLDYGIYVIHQAEKKFNRAKLLNVGYLEALKEEN  
WDCFIFHDVDLVPENDFNLYKCEEHPKHLVVGRNSTGYRLRYSGYFGGVTALSREQFFKVNG  
FSNNYWGWWGEGDDDLRLRVELQRMKISRPLPEVGKYTMVFHTRDKGNEVNAERMKLLHQVSR  
VWRTDGLSSCSYKLVSVEHNPLYINITVDFWFGA

**Important features:**

**Signal peptide:**

amino acids 1-27

**N-glycosylation sites:**

amino acids 4-7, 220-223 and 335-338

**Xylose isomerase proteins:**

amino acids 191-201

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FIGURE 162

CGTGGGCCGGGGTTCGCGCAGCGGGCTGTGGGCGCGCCCGGAGGAGCGACCGCCGAGTTCTC  
GAGCTCCAGCTGCATTCCCTCCGCGTCCGCCCCACGCTTCTCCGCTCCGGGCCCCGCAATG  
GCCCAGGCAGTGTGGTCCGCGCTCGGCCGCATCCTCTGGCTTGCTGCCTCCTGCCCTGGGC  
CCCGGCAGGGGTGGCCGAGGCCTGTATGAACTCAATCTCACCACCGATAGCCCTGCCACCA  
CGGGAGCGGTGGTGACCATCTCGGCCAGCCTGGTGGCCAAGGACAACGGCAGCCTGGCCCTG  
CCCGCTGACGCCCACCTCTACCGCTTCCACTGGATCCACACCCCGCTGGTGCTTACTGGCAA  
GATGGAGAAGGGTCTCAGCTCCACCATCCGTGTGGTCCGCCACGTGCCCGGGGAATTCCCGG  
TCTCTGTCTGGGTCACTGCCGCTGACTGCTGGATGTGCCAGCCTGTGGCCAGGGGCTTTGTG  
GTCTCCCCATCACAGAGTTCTCGTGGGGGACCTTGTTGTACCCAGAACAATTCCCTACC  
CTGGCCAGCTCCTATCTCACTAAGACCGTCTGAAAGTCTCCTTCTCTCCACGACCCGA  
GCAACTTCTCAAGACCGCTTGTCTCTACAGCTGGGACTTCGGGGACGGGACCCAGATG  
GTGACTGAAGACTCCGTGGTCTATTATAAATTCCATCATCGGGACCTTCACCGTGAAGCT  
CAAACTGGTGGCGAGTGGGAAGAGGTGGAGCCGGATGCCACGAGGGCTGTGAAGCAGAAGA  
CCGGGGACTTCTCCGCTCGCTGAAGCTGCAGGAAACCCTTCGAGGCATCCAAGTGTGGGG  
CCCACCTAATTGAGACCTTCCAAAAGATGACCGTGACCTTGAAGTCTCTGGGGAGCCCTCC  
TCTGACTGTGTGCTGGCTCTCAAGCCTGAGTGCCTCCCGCTGGAGGAAGGGGAGTGCCACC  
CTGTGTCCGTGGCCAGCACAGCGTACAACCTGACCCACACCTTCAGGGACCTTGGGGACTAC  
TGCTTCAGCATCCGGGCCGAGAATATCATCAGCAAGACACATCAGTACCACAAGATCCAGGT  
GTGGCCCTCCAGAATCCAGCCGGCTGTCTTGCTTCCCATGTGCTACACTTATCACTGTGA  
TGTTGGCCTTCATCATGTACATGACCCTGCGGAATGCCACTCAGCAAAAGGACATGGTGGAG  
AACCCGGAGCCACCCTCTGGGGTCAAGTGTGCTGCCAGATGTGCTGTGGGCCCTTCTTGCT  
GGAGACTCCATCTGAGTACCTGGAAATTGTTCTGTGAGAACCACGGGCTGCTCCCGCCCTCT  
ATAAGTCTGTCAAACTTACACCGTGTGAGCACTCCCCCTCCCCACCCATCTCAGTGTTAA  
CTGACTGCTGACTTGGAGTTTCAGCAGGGTGGTGTGCACCACTGACCAGGAGGGGTTCATT  
TGCGTGGGGCTGTTGGCCTGGATCATCCATCCATCTGTACAGTTCAAGCACTGCCACAAGCC  
CCTCCCTCTCTGTACCCCTGACCCAGCCATTCACCCATCTGTACAGTCCAGCCACTGACA  
TAAGCCCCACTCGGTTACCACCCCTTGACCCCTACCTTTGAAGAGGCTTCGTGCAGGACT  
TTGATGCTTGGGGTGTTCCTGTGACTCCTAGGTGGGCCTGGCTGCCCACTGCCCATTCCT  
CTCATATTGGCACATCTGCTGTCCATTGGGGGTCTCAGTTTCTCCCCCAGACAGCCCTAC  
CTGTGCCAGAGAGCTAGAAAGAAGGTCTAAAGGGTTAAAAATCCATAACTAAAGGTTGTAC  
ACATAGATGGGCACACTCACAGAGAGAAGTGTGCATGTACACACACCACACACACACACA  
CACACACACACAGAAATATAAACACATGCGTCACATGGGCATTTTCAGATGATCAGCTCTGTA  
TCTGGTTAAGTCGGTTGCTGGGATGCACCCTGCACTAGAGCTGAAAGGAAATTTGACCTCCA  
AGCAGCCCTGACAGGTTCTGGGCCCGGGCCCTCCCTTTGTGCTTTGTCTCTGCAAGTTCTTGC  
GCCCTTTATAAGGCCATCCTAGTCCCTGCTGGCTGGCAGGGGCTGGATGGGGGGCAGGACT  
AATACTGAGTGATTGCAGAGTGCTTTATAAATATCACCTTATTTTATCGAAACCCATCTGTG  
AAACTTTCACTGAGGAAAAGGCCTTGACGCGGTAGAAGAGGTTGAGTCAAGGCCGGCGCGG  
TGGCTCACGCCTGTAATCCAGCACTTTGGGAGGCCGAGGCGGGTGGATCACGAGATCAGGA  
GATCGAGACCACCTGGCTAACACGGTGAAACCCCGTCTCTACTAAAAAATACAAAAAGTT  
AGCCGGGCGTGGTGGTGGTGCCTGTAGTCCAGCTACTCGGGAGGCTGAGGCAGGAGAATG  
GTGCGAACCCGGGAGGCGGAGCTTGAGTGAAGCCAGATGGCGCCACTGCACTCCAGCCTGA  
GTGACAGAGCGAGACTCTGTCTCCA

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FIGURE 163

MAQAVWSRLGRILWLACLLPWAPAGVAAGLYELNLTTDSPATTGAVVTISASLVAKDNGSLA  
LPADAHLYRFHWIHTPLVLTGKMEKGLSSTIRVVGHPGEFPVSVWVTAADCWMCQPVARGF  
VVLPITEFLVGDLVVTQNTSLPWPSYLTKTVLKVSFLLHDPSNFLKTALFLYSWDFGDGTQ  
MVTEDSVVYYNYSIIIGTFTVKLKVVAEWEEVEPDATRAVKQKTGDFSASLKLQETLRGIQVL  
GPTLIQTFQKMTVTNLNGLSPPLTVCWRLKPECLPLEEGECHPVSVASTAYNLTHTRDPGD  
YCFSIRAENIISKTHQYHKIQVWPSRIQPAVFAPPCATLITVMLAFIMYMTLRNATQQKDMV  
ENPEPPSGVRCCCOMCCGPFLLETPSEYLEIVRENHGLLPPLYKSVKTYTV

**Important features of the protein:**

**Signal peptide:**

amino acids 1-24

**Transmembrane domain:**

amino acids 339-362

**N-glycosylation sites.**

amino acids 34-37, 58-61, 142-145, 197-200, 300-303 and 364-367





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FIGURE 165

MALESSQIWAACLLLLLLLLASLTSCSVFPQQTGQLAELQPQDRAGARASWMPMFQRRRRRRDTH  
FPICIFCCGCCHRSKCGMCCKT

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FIGURE 166

CTGTCAGGAAGGACCATCTGAAGGCTGCAATTTGTTCTTAGGGAGGCAGGTGCTGGCCTGGC  
CTGGATCTTCCACCATGTTTCCTGTTGCTGCCTTTTGATAGCCTGATTGTCAACCTTCTGGGC  
ATCTCCCTGACTGTCTCTTCCACCTCCTTCTCGTTTTTCATCATAGTGCCAGCCATTTTTGG  
AGTCTCCTTTGGTATCCGCAAACCTACATGAAAAGTCTGTTAAAAATCTTTGCGTGGGCTA  
CCTTGAGAATGGAGCGAGGAGCCAAGGAGAAGAACCACCAGCTTTACAAGCCCTACACCAAC  
GGAATCATTGCAAAGGATCCCACTTCACTAGAAGAAGAGATCAAAGAGATTCTCGAAGTGG  
TAGTAGTAAGGCTCTGGACAACACTCCAGAGTTCGAGCTCTCTGACATTTTCTACTTTTGGC  
GGAAAGGAATGGAGACCATTATGGATGATGAGGTGACAAAGAGATTCTCAGCAGAAGAACTG  
GAGTCTTGGAACCTGCTGAGCAGAACCAATTATAACTTCCAGTACATCAGCCTTCGGCTCAC  
GGTCTTGGGGGTTAGGAGTGCTGATTTCGGTACTGCTTTCTGCTGCCGCTCAGGATAGCAC  
TGGCTTTTACAGGGATTAGCCTTCTGGTGGTGGGCACAACTGTGGTGGGATACTTGCCAAAT  
GGGAGGTTTAAAGGAATTCATGAGTAAACATGTTCACTTAATGTGTTACCGGATCTGCGTGCG  
AGCGCTGACAGCCATCATCACCTACCATGACAGGGAAAACAGACCAAGAAATGGTGGCATCT  
GTGTGGCCAATCATACCTCACCGATCGATGTGATCATCTTGGCCAGCGATGGCTATTATGCC  
ATGGTGGGTCAAGTGACAGGGGGACTCATGGGTGTGATTGAGAGAGCCATGGTGAAGCCCTG  
CCCACACGTCCTGTTTTGAGCGCTCGGAAGTGAAGGATCGCCACCTGGTGGCTAAGAGACTGA  
CTGAACATGTGCAAGATAAAAGCAAGCTGCCTATCCTCATCTTCCCAGAAGGAACCTGCATC  
AATAATACATCGGTGATGATGTTCAAAAAAGGGAAGTTTTGAAATTGGAGCCACAGTTTACCC  
TGTTGCTATCAAGTATGACCCCTCAATTTGGCGATGCCTTCTGGAACAGCAGCAAATACGGGA  
TGGTGACGTACCTGCTGCGAATGATGACCAGCTGGGCCATTGTCTGCAGCGTGTGGTACCTG  
CCTCCCATGACTAGAGAGGCAGATGAAGATGCTGTCCAGTTTGGCAATAGGGTGAAATCTGC  
CATTGCCAGGCAGGGAGGACTTGTGGACCTGCTGTGGGATGGGGCCCTGAAGAGGGAGAAGG  
TGAAGGACACGTTCAAGGAGGAGCAGCAGAAGCTGTACAGCAAGATGATCGTGGGGAACAC  
AAGGACAGGAGCCGCTCTGAGCCTGCCTCCAGCTGGCTGGGGCCACCGTGCGGGGTGCCAA  
CGGGCTCAGAGCTGGAGTTGCCGCCGCCGCCCTGCTGTGTCTTTCCAGACTCCAGGG  
CTCCCCGGGCTGCTCTGGATCCCAGGACTCCGGCTTTCGCCGAGCCGCAGCGGGATCCCTGT  
GCACCCGGCGCAGCCTACCCCTGGTGGTCTAAACGGATGCTGCTGGGTGTTGCGACCCAGGA  
CGAGATGCCTTGTTTCTTTTACAATAAGTCGTTGGAGGAATGCCATTAAAGTGAACCCCCA  
CCTTTGCACGCTGTGCGGGCTGAGTGGTTGGGGAGATGTGGCCATGGTCTTGTGCTAGAGAT  
GGCGGTACAAGAGTCTGTTATGCAAGCCCGTGTGCCAGGGATGTGCTGGGGGCGGCCACCCG  
CTCTCCAGGAAAGGCACAGCTGAGGCACTGTGGCTGGCTTCGGCCTCAACATCGCCCCCAGC  
CTTGGAGCTCTGCAGACATGATAGGAAGGAACTGTCATCTGCAGGGGCTTTTCAAGAAAATG  
AAGGGTTAGATTTTTATGCTGCTGCTGATGGGGTTACTAAAGGGAGGGGAAGAGGCCAGGTG  
GGCCGCTGACTGGGCCATGGGGAGAACGTGTGTTCTGACTCCAGGCTAACCTGAACTCCCC  
ATGTGATGCGCGCTTTGTTGAATGTGTGCTCGGTTTCCCATCTGTAATATGAGTCGGGGG  
GAATGGTGGTGATTCCCTACCTCACAGGGCTGTTGTGGGGATTAAAGTGCTGCGGGTGAGTGA  
AGGACACATCACGTTCAAGTACAGGCCCAAAAACGGGGCACGGCAGGCCCTGAG  
CTCAGAGCTGCTGCACTGGGCTTTGGATTTGTTCTTGTGAGTAAATAAACTGGCTGGTGAATGA

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FIGURE 167

MFLLLPFDSLIVNLDGISLTVLFTLLLVFTIIVPAIFGVVSFGIRKLYMKSLKIFAWATLRME  
RGAKEKNHQLYKPYTNGIIAKDPTSLEEEIKEIRRS GSSKALDNTPEFELSDIFYFCRKGME  
TIMDDEVTKRFSAEELSWNLLSRTNYNFYISLRLTVLWGLGVLIRYCFLLPLRIALFTG  
ISLLVVGTTVVGYLPNGRFKEFMSKHVHLMCYRICVRALTAIITYHDRENRPNGGICVANH  
TSPIDVIIILASDGYAMVGQVHGGLMGVIQAMVKACPHVWFERSEVKDRHLVAKRLTEHVQ  
DKSKLPILIFPEGTCINNTSVMMFKKGSFEIGATVYPVAIKYDPQFGDAFWNSSKYGMVTYL  
LRMTSWAIVCSVWYLPMTREADEDAVQFANRVKSAIARQGGLVDLLWDGGLKREKVKDTF  
KEEQKLYSKMIVGNHKDRSRS

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FIGURE 168

GCCCCTCGAAACCAGGACTCCAGCACCTCTGGTCCCCGCCCTCACCCGGACCCCTGGCCCTCA  
CGTCTCCTCCAGGGATGGCGCTGGCGGCTTTGATGATCGCCCTCGGCAGCCTCGGCCTCCAC  
ACCTGGCAGGCCCCAGGCTGTTCCACCATCCTGCCCCCTGGGCCTGGCTCCAGACACCTTTGA  
CGATACCTATGTGGGTTGTGCAGAGGAGATGGAGGAGAAGGCAGCCCCCTGCTAAAGGAGG  
AAATGGCCCACCATGCCCTGCTGCCGGAATCCTGGGAGGCAGCCAGGAGACCTGGGAGGAC  
AAGCGTCGAGGGCTTACCTTGCCCCCTGGCTTCAAAGCCCAGAATGGAATAGCCATTATGGT  
CTACACCAACTCATCGAACACCTTGTACTGGGAGTTGAATCAGGCCGTGCGGACGGGCGGAG  
GCTCCCGGGAGCTCTACATGAGGCACCTTCCCTTCAAGGCCCTGCATTTCTACCTGATCCG  
GCCCTGCAGCTGCTGCGAGGCAGTGGGGGCTGCAGCAGGGGACCTGGGGAGGTGGTGTTCG  
AGGTGTGGGCAGCCTTCGCTTTGAACCCAAGAGGCTGGGGGACTCTGTCCGCTTGGGCCAGT  
TTGCCTCCAGCTCCCTGGATAAAGCAGTGGCCACAGATTTGGGGAGAAGAGGCGGGGCTGT  
GTGTCTGCGCCAGGGGTGCAGCTAGGGTCACAATCTGAGGGGGCCTCCTCTCTGCCCCCTG  
GAAGACTCTGCTCTTGGCCCCCTGGAGAGTTCCAGCTCTCAGGGGTGGGGCCCTGAAAGTCCA  
ACATCTGCCACTTAGGAGCCCTGGGAACGGGTGACCTTCATATGACGAAGAGGCACCTCCAG  
CAGCCTTGAGAAGCAAGAACATGGTTCCGGACCCAGCCCTAGCAGCCTTCTCCCCAACCCAGG  
ATGTTGGCCTGGGGAGGCCACAGCAGGGCTGAGGGAACCTCTGCTATGTGATGGGGACTTCCT  
GGGACAAGCAAGGAAAGTACTGAGGCAGCCACTTGATTGAACGGTGTGCAATGTGGAGACA  
TGGAGTTTTATTGAGGTAGCTACGTGATTAAATGGTATTGCAGTGTGGA

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FIGURE 169

MALAALMIALGSLGLHTWQAQAVPTILPLGLAPDTFDDTYVGCAEEMEEKAAPLLKEEMAHH  
ALLRESWEAAQETWEDKRRGLTLPFGFKAQNGIAIMVYTNSSNTLYWELNQAVRTGGGSREL  
YMRHFFKALHFYLIRALQLLRGSGGCSRGPGEVVFRGVGSLRFEPKRLGDSVRLGQFASSS  
LDKAVAHRFGEKRRGCVSAPGVQLGSQSEGASSLPPWKTLLLAPGEFQLSGVGP

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FIGURE 170

GTGGCTTCATTTTCAGTGGCTGACTTCCAGAGAGCAATATGGCTGGTTCCCCAACATGCCTCA  
CCCTCATCTATATCCTTTGGCAGCTCACAGGGTCAGCAGCCTCTGGACCCGTGAAAGAGCTG  
GTCGGTTCCGTTGGTGGGGCCGTGACTTTCCCCCTGAAGTCCAAAGTAAAGCAAGTTGACTC  
TATTGTCTGGACCTTCAACACAACCCCTCTTGTCAACCATAAGCCAGAGGGGGGCACTATCA  
TAGTGACCCAAAATCGTAATAGGGAGAGAGTAGACTTCCCAGATGGAGGCTACTCCCTGAAG  
CTCAGCAAACCTGAAGAAGAATGACTCAGGGATCTACTATGTGGGGATATACAGCTCATCACT  
CCAGCAGCCCTCCACCCAGGAGTACGTGCTGCATGTCTACGAGCACCTGTCAAAGCCTAAAG  
TCACCATGGGTCTGCAGAGCAATAAGAATGGCACCTGTGTGACCAATCTGACATGCTGCATG  
GAACATGGGGAAGAGGATGTGATTTATACCTGGAAGGCCCTGGGGCAAGCAGCCAATGAGTC  
CCATAATGGGTCCATCCTCCCCATCTCCTGGAGATGGGGAGAAAGTGATATGACCTTCATCT  
GCGTTGCCAGGAACCCTGTCAGCAGAACTTCTCAAGCCCCATCCTTGCCAGGAAGCTCTGT  
GAAGGTGCTGCTGATGACCCAGATTCTCCATGGTCCTCCTGTGTCTCCTGTTGGTGGCCCT  
CCTGCTCAGTCTCTTTGTACTGGGGCTATTTCTTTGGTTTCTGAAGAGAGAGAGACAAGAAG  
AGTACATTGAAGAGAAGAAGAGAGTGGACATTTGTGCGGAAACTCCTAACATATGCCCCCAT  
TCTGGAGAGAACACAGAGTACGACACAATCCCTCACACTAATAGAACAAATCCTAAAGGAAGA  
TCCAGCAAATACGGTTTACTCCACTGTGGAAATACCGAAAAAGATGGAAAATCCCCACTCAC  
TGCTCACGATGCCAGACACACCAAGGCTATTTGCCTATGAGAATGTTATCTAGACAGCAGTG  
CACTCCCCTAAGTCTCTGCTCA

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FIGURE 171

MAGSPTCLTLIYILWQLTGSAASGPVKELVGSVGGAVTFPLKSKVKQVDSIVWTFNTTPLVT  
IQPEGGTIIIVTQNRNRERVDFPDGGYSLKLSKLKKNDSGIYYVGIYSSSLQQPSTQEYVLHV  
YEHLSPKVTMGLQSNKNGTCVTNLTCMEHGEEDVIYTWKALGQAANESHNGSILPISWRW  
GESDMTFICVARNPVSRNFSSPILARKLCEGAADDPDSSMVLLCLLLVPLLLSLFVLGLFLW  
FLKRERQEEYIEKKRVDICRETPNICPHSGENTHEYDTIPHTNRTILKEDPANTVYSTVEIP  
KKMENPHSLLTMPDTPRLFAYENVI

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FIGURE 172

CTGGTTCCCCAACATGCCTCACCCCTCATCTATATCCTTTGGCAGCTCACAGGGTCAGCAGCC  
TCTGGACCCCGTGAAAGAGCTGGTCGGTTCCGTTGGTGGGGCCGTGACTTTCCCCCTGAAGTC  
CAAAGTAAAGCAAGTTGACTCTATTGTCTGGACCTTCAACACAACCCCTCTTGTCACCATAC  
AGCCAGAAGGGGGCACTATCATAGTGACCCAAAATCGTAATAGGGAGAGAGTAGACTTCCCA  
GATGGAGGCTACTCCCTGAAGCTCAGCAAACCTGAAGAAGAATGACTCAGGGATCTACTATGT  
GGGGATATACAGCTCATCACTCCAGCAGCCCTCCACCCAGGAGTACGTGCTGCATGTCTACG  
AGCACCTGTCAAAGCCTAAAGTCACCATGGGTCTGCAGAGCAATAAGAATGGCACCTGTGTG  
ACCAATCTGACATGCTGCATGGAACATGGGGAAGAGGATGTGATTTATACCTGGAAGGCCCT  
GGGGCAAGCAGCCAATGAGTCCCATAATGGGTCCATCCTCCCCATCTCCTGGAGATGGGGAG  
AAAGTGATATGACCTTCATCTGCGTTGCCAGGAACCCTGTCAGCAGAACTTCTCAAGCCCC  
ATCCTTGCCAGGAAGCTCTGTGAAGGTGCTGCTGATGACCCAGATTCTCCATGGTCTCTCT  
GTGTCTCCTGTTGGTGCCCCCTCCTGCTCAGTCTCTTTGTACTGGGGCTATTTCTTTGGTTTC  
TGAAGAGAGAGAGACAAGAAGAGTACATTGAAGAGAAGAAGAGAGTGGACATTTGTCTGGGAA  
ACTCCTAACATATGCCCCCATCTGGAGAGAACACAGAGTACGACACAATCCCTCACACTAA  
TAGAACAATCCTAAAGGAAGATCCAGCAAATACGGTTTACTCCACTGTGGAAATACCGAAAA  
AGATGGAAAATCCCCACTCACTGCTCACGATGCCAGACACACCAAGGCTATTTGCCTATGAG  
AATGTTATCTAGACAGCAGTGCCTCCCCTAAGTCTCTGCTCAAAAAAAAAAAAAAAAAAAAA



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FIGURE 173

GAAAGACGTGGTCCTGACAGACAGACAATCCTATTCCCTACCAAAATGAAGATGCTGCTGCT  
GCTGTGTTTGGGACTGACCCTAGTCTGTGTCCATGCAGAAGAAGCTAGTTCTACGGGAAGGA  
ACTTTAATGTAGAAAAGATTAATGGGGAATGGCATACTATTATCCTGGCCTCTGACAAAAGA  
GAAAAGATAGAAGAACATGGCAACTTTAGACTTTTTCTGGAGCAAATCCATGTCTTGAGAGAA  
TTCCTTAGTTCTTAAAGTCCATACTGTAAGAGATGAAGAGTGCTCCGAATTATCTATGGTTG  
CTGACAAAACAGAAAAGGCTGGTGAATATTCTGTGACGTATGATGGATTCAATACATTTACT  
ATACCTAAGACAGACTATGATAACTTTCTTATGGCTCACCTCATTAACGAAAAGGATGGGGA  
AACCTTCCAGCTGATGGGGCTCTATGGCCGAGAACCAGATTTGAGTTCAGACATCAAGGAAA  
GGTTTGCACACTATGTGAGGAGCATGGAATCCTTAGAGAAAATATCATTGACCTATCCAAT  
GCCAATCGCTGCCTCCAGGCCCGAGAATGAAGAATGGCCTGAGCCTCCAGTGTTGAGTGAC  
ACTTCTCACCAGGACTCCACCATCATCCCTTCCTATCCATACAGCATCCCCAGTATAAATTC  
TGTGATCTGCATTCCATCCTGTCTCACTGAGAAGTCCAATTCAGTCTATCAACATGTTACC  
TAGGATACCTCATCAAGAATCAAAGACTTCTTTAAATTTCTCTTTGATACACCCCTTGACAAT  
TTTTCATGAAATTATTCCTCTTCCTGTTCAATAAATGATTACCCTTGCACTTAA

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**FIGURE 174**

MKMLLLLCLGLTLVCVHAEASSTGRNFNVEKINGEWHTIILASDKREKIEEHGNFRLFLEQ  
IHVLENSLVLVKVTVRDEECSELSMVADKTEKAGEYSVTYDGFNTFTIPKTDYDNFLMAHLI  
NEKDGETFQLMGLYGREPDLSSEIKERFAQLCEEHGILRENIIDLSNANRCLQARE

FIGURE 175

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**FIGURE 176**

MTCCEGWTSCNGFSLLVLLLLGVVLNAIPLIVSLVEEDQFSQNPISCFEWWFPGIIGAGLMA  
IPATTMSLTARKRACCNNRTGMFLSSFFSVITVIGALYCMLISIQALLKGPLMCNPSNSNA  
NCEFSLKNISDIHPESFNLQWFFNDSCAPPTGFNKPTSNDTMASGWRASSFHFDFSEENKHRL  
IHFSVFLGLLLVGILEVLFGLSQIVIGFLGCLCGVSKRRSQIV

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FIGURE 177

GTCGAATCCAAATCACTCATTGTGAAAGCTGAGCTCACAGCCGAATAAGCCACCAATGAGGCT  
GTCAGTGTGTCTCCTGATGGTCTCGCTGGCCCTTTGCTGCTACCAGGCCCCATGCTCTTGTCT  
GCCCAGCTGTTGCTTCTGAGATCACAGTCTTCTTATTCTTAAGTGACGCTGCGGTAAACCTC  
CAAGTTGCCAAACTTAATCCACCTCCAGAAGCTCTTGCAGCCAAGTTGGAAGTGAAGCACTG  
CACCGATCAGATATCTTTTAAGAAACGACTCTCATTGAAAAAGTCCTGGTGGAAATAGTGAA  
AAAATGTGGTGTGTGACATGTAAAAATGCTCAACCTGGTTTCCAAAGTCTTTCAACGACACC  
CTGATCTTCACTAAAAATTGTAAAGGTTTCAACACGTTGCTTTAATAAATCACTTGCCCTGC

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**FIGURE 178**

MRLSVCLLMVSLALCCYQAHALVCPAVASEITVFLFLSDAAVNLQVAKLNPPPEALAAKLEV  
KHCTDQISFKKRLSLKKSWWK

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FIGURE 179

ATCCGTTCTCTGCGCTGCCAGCTCAGGTGAGCCCTCGCCAAGGTGACCTCGCAGGACACTGG  
TGAAGGAGCAGTGAGGAACCTGCAGAGTCACACAGTTGCTGACCAATTGAGCTGTGAGCCTG  
GAGCAGATCCGTGGGCTGCAGACCCCCGCCCCAGTGCCTCTCCCCCTGCAGCCCTGCCCCCTC  
GAACTGTGACATGGAGAGAGTGACCCTGGCCCTTCTCCTACTGGCAGGCCTGACTGCCTTGG  
AAGCCAATGACCCATTTGCCAATAAAGACGATCCCTTCTACTATGACTGGAAAAACCTGCAG  
CTGAGCGGACTGATCTGCGGAGGGCTCCTGGCCATTGCTGGGATCGCGGCAGTTCTGAGTGG  
CAAATGCAAATACAAGAGCAGCCAGAAGCAGCACAGTCCTGTACCTGAGAAGGCCATCCCAC  
TCATCACTCCAGGCTCTGCCACTACTTGCTTGAGCACAGGACTGGCCTCCAGGGATGGCCTGA  
AGCCTAACACTGGCCCCCAGCACCTCCTCCCCCTGGGAGGCCTTATCCTCAAGGAAGGACTTC  
TCTCCAAGGGCAGGCTGTTAGGCCCTTTCTGATCAGGAGGCTTCTTTATGAATTAAACTCG  
CCCCACCACCCCTCA

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**FIGURE 180**

MERVTLALLLLAGLTALEANDPFANKDDPFYYDWKNLQLSGLICGGLLAIAAGIAAVLSGKCK  
YKSSQKQHSPVPEKAIPILITPGSATTC



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FIGURE 181

GGAGAAGAGGTTGTGTGGGACAAGCTGCTCCCGACAGAAGGATGTCGCTGCTGAGCCTGCCC  
TGGCTGGGCCTCAGACCGGTGGCAATGTCCCCATGGCTACTCCTGCTGCTGGTTGTGGGCTC  
CTGGCTACTCGCCCGCATCCTGGCTTGGACCTATGCCTTCTATAACAACTGCCGCCGGCTCC  
AGTGTTTCCACAGCCCCCAAACGGAACTGGTTTTGGGGTCACCTGGGCCTGATCACTCCT  
ACAGAGGAGGGCTTGAAGGACTCGACCCAGATGTGGCCACCTATTCCAGGGCTTTACGGT  
ATGGCTGGGTCCCATCATCCCCTTCATCGTTTTATGCCACCCTGACACCATCCGGTCTATCA  
CCAATGCCTCAGCTGCCATTGCACCCAAGGATAATCTCTTCATCAGGTTCTGAAGCCCTGG  
CTGGGAGAAGGGATACTGCTGAGTGGCGGTGACAAGTGGAGCCGCCACCGTCGGATGCTGAC  
GCCCCCCTTCCATTTCAACATCCTGAAGTCCTATATAACGATCTTCAACAAGAGTGCAACA  
TCATGCTTGACAAGTGGCAGCACCTGGCCTCAGAGGGCAGCAGTCGTCTGGACATGTTTGAG  
CACATCAGCCTCATGACCTTGGACAGTCTACAGAAATGCATCTTCAGCTTTGACAGCCATTG  
TCAGGAGAGGCCAGTGAATATATTGCCACCATCTTGGAGCTCAGTGCCCTTGAGAGAAAA  
GAAGCCAGCATATCCTCCAGCACATGGACTTTCTGTATTACCTCTCCCATGACGGGCGGCGC  
TTCCACAGGGCCTGCCGCTGGTGCATGACTTCACAGACGCTGTATCCGGGAGCGGCGTCG  
CACCTCCCCACTCAGGGTATTGATGATTTTTTCAAAGACAAAGCCAAGTCCAAGACTTTGG  
ATTTTCATTGATGTGCTTCTGCTGAGCAAGGATGAAGATGGGAAGGCATTGTCAGATGAGGAT  
ATAAGAGCAGAGGCTGACACCTTCATGTTTGGAGGCCATGACACCACGGCCAGTGGCCTCTC  
CTGGGTCTGTACAACCTTGCGAGGCACCCAGAATACCAGGAGCGCTGCCGACAGGAGGTGC  
AAGAGCTTCTGAAGGACCGGATCCTAAAGAGATTGAATGGGACGACCTGGCCCAGCTGCCC  
TTCCTGACCATGTGCGTGAAGGAGAGCCTGAGGTTACATCCCCCAGCTCCCTTCATCTCCCG  
ATGCTGCACCCAGGACATTGTTCTCCAGATGGCCGAGTCATCCCCAAAGGCATTACCTGCC  
TCATCGATATTATAGGGGTCCATCACAACCCAACTGTGTGGCCGGATCCTGAGGTCTACGAC  
CCCTTCCGCTTTGACCCAGAGAACAGCAAGGGGAGGTACCTCTGGCTTTTATTCTTTCTC  
CGCAGGGCCCAGGAACATGCATCGGGCAGGCGTTTCGCCATGGCGGAGATGAAAGTGGTCCTGG  
CGTTGATGCTGCTGCACCTTCCGGTTCCCTGCCAGACCACACTGAGCCCCGAGGAAGCTGGAA  
TTGATCATGCGCGCCGAGGGCGGGCTTTGGCTGCGGGTGGAGCCCCGAAATGTAGGCTTGCA  
GTGACTTTCTGACCCATCCACCTGTTTTTTTGCAGATTGTCATGAATAAAACGGTGCTGTCAAA

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FIGURE 182

MSLLSLPWLGLRPVAMSPWLLLLLVVGSWLLARILAWTYAFYNNCRRLQCFPPKRNWFWG  
HLGLITPTEEGLKDSTQMSATYSQGFTVWLGPIIPFIVLCHPDTIRSITNASAAIAPKDNLF  
IRFLKPWLGEKILLSGGDKWSRHRRLTPAFHFNILKSYITIFNKSANIMLDKWQHASEGS  
SRLDMFEHISLMTLDSLQKCIFSFDSHCQERPSEYIATILELSALVEKRSQHILQHMDFLYY  
LSHDGRRFHRACRLVHDFDVAIRERRRRLTPTQGIDDFKDKAKSKTLDFIDVLLLSKDEG  
KALSDEDIRAEADTFMFGGHDTTASGLSWVLYNLARHPEYQERCQEVQELLKDRDPKEIEW  
DDLAQLPFLTMCVKESLRLHPPAPFISRCCTQDIVLPDGRVIPKGITCLIDIIGVHHNPTVW  
PDPEVYDPFRFDPENSKGRSPLAFIPFSAGPRNCIGQAFAMAEMKVVLALMLLHFRFLPDHT  
EPRRKLELIMRAEGGLWLRVEPLNVGLQ

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FIGURE 183

CAACAGAAGCCAAGAAGGAAGCCGTCTATCTTGTGGCGATCATGTATAAGCTGGCCTCCTGC  
TGTTTGCTTTTCACAGGATTCTTAAATCCTCTCTTATCTCTTCCTCTCCTTGACTCCAGGGA  
AATATCCTTTCAACTCTCAGCACCTCATGAAGACGCGCGCTTAACTCCGGAGGAGCTAGAAA  
GAGCTTCCCTTCTACAGATATTGCCAGAGATGCTGGGTGCAGAAAGAGGGGATATTCTCAGG  
AAAGCAGACTCAAGTACCAACATTTTTAACCCAAGAGGAAATTTGAGAAAGTTTCAGGATTT  
CTCTGGACAAGATCCTAACATTTTACTGAGTCATCTTTGGCCAGAATCTGGAAACCATACA  
AGAAACGTGAGACTCCTGATTGCTTCTGGAAATACTGTGTCTGAAGTGAAATAAGCATCTGT  
TAGTCAGCTCAGAAACACCCATCTTAGAATATGAAAAATAACACAATGCTTGATTTGAAAAC  
AGTGTGGAGAAAACTAGGCAAACTACACCCTGTTTATTGTTACCTGGAAAATAAATCCTCT  
ATGTTTTGCACAAAAAAAAAAAAAAAAA

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**FIGURE 184**

MYKLASCCLLFTGFLNPLLSLPLLDREISFQLSAPHEDARLTPEELERASLLQILPEMLGA  
ERGDILRKADSSTNIFNPRGNLRKFQDFSGQDPNILLSHLLARIWKPYKKRETPDCFWKYCV

FIGURE 185

GAACATTTTGTAGTTCCCAAGGAATGTACATCAGCCCCACGGAAGCTAGGCCACCTCTGGGAT  
GGGGTTGCTGGTTTAAAACAAACGCCAGTCATCCTATATAAGGACCTGACAGCCACCAGGCA  
CCACCTCCGCCAGGAAGTGCAGGCCCCACCTGTCTGCAACCCAGCTGAGGCCATGCCCTCCCC  
AGGGACCGTCTGCAGCCTCCTGCTCCTCGGCATGCTCTGGCTGGACTTGGCCATGGCAGGCT  
CCAGCTTCCTGAGCCCTGAACACCAGAGAGTCCAGCAGAGAAAGGAGTCCAAGAAGCCACCA  
GCCAAGCTGCAGCCCCGAGCTCTAGCAGGCTGGCTCCGCCCCGGAAGATGGAGGTCAAGCAGA  
AGGGGCAGAGGATGAACTGGAAGTCCGGTTCAACGCCCCCTTTGATGTTGGAATCAAGCTGT  
CAGGGGTTCAGTACCAGCAGCACAGCCAGGCCCTGGGGAAGTTTCTTCAGGACATCCTCTGG  
GAAGAGGCCAAAGAGGCCCCAGCCGACAAGTGAATCGCCCCACAAGCCTTACTCACCTCTCTCT  
AAGTTTAGAAGCGCTCATCTGGCTTTTCGCTTGCTTCTGCAGCAACTCCCACGACTGTTGTA  
CAAGCTCAGGAGGCGAATAAATGTTCAAAGTCTGTA

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**FIGURE 186**

MPSPGTVCSLLLLGMLWLDLAMAGSSFLSPEHQRVQQRKESKKPPAKLQPRALAGWLRPEDG

GQAEGAEDELEVRFNAPFDVGIKLSGVQYQQHSQALGKFLQDILWEEAKEAPADKO

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**FIGURE 187**

CGGCCACAGCTGGCATGCTCTGCCTGATCGCCATCCTGCTGTATGTCCTCGTCCAGTACCTC  
GTGAACCCCGGGGTGCTCCGCACGGACCCCAGATGTCAAGAATATGAACACGTGGCTGCTGT  
TCCTCCCCCTGTTCCCGGTGCAGGTGCAGACCCTGATAGTCGTGATCATCGGGATGCTCGTG  
CTCTGCTGGACTTTCTTGCTTGGTGCACCTGGGCCAGCTGCTCATCTTCCACATCTACCT  
GAGTATGTCCCCACCCCTAAGCCCCCGATCCCCCAAGGCTGGGTGGTCAGAGCTGCTCATC  
TTACACCTCTACTTGAGTATGTCCCTAACCCCTGAGCCCCCACGCCCTGGGGCCAGAGTCTTT  
GTCCCCCGTGTGCGCATGTGTTTCAAGGTGAGCCTCTCCAGAAGTGAGATCATGGACAAAAA  
GGGCAAATCACAGGAAGAAATTAAATCCATGAGGACCCAGCAGGCCCAAGAAGCTGAAC  
TCACGCCGAGACCTGCAGGAGTGGTGCCAGGTGCTTGAAGTAACAAGTTTAAAAATGTTTCA  
GACAATGGAATGGAATCTATTAGGCAAGAACAGGACATTATGAAATAAGGACAGGTGGACTT  
CCAAAAACACAAGTAGAAATTCTAACAAATGAAATATATTACAGGCAGGTCACCCCTAACCA  
AACAACTGAAGCGAGAGCTGTGGTCTTGCTTGGTCTCACAGTGGGCACAGCGGTAGGCGGTC  
AGTCATGTTGCTGAACGACGGAGGGTAAACTCCCCAGCCCCAAGAAAACCTGTGTTGGAAGT  
AACAAACACCTCCCTGCTCCTGGCACCAGCCGTTTTTGGTCATGGTGGGCCAGCTGCAAAGCG  
TCTTCCATTCTCTGGGCAGTGGTGGCCCCGAGGCTGTGGCCTCTCAGGGGGTTTCTGTGGAC  
ACGGGCAGCAGAGTGTGTCCAGGCCAGCCCCCAAGAATGCCCTGCTCCTGACAGCTTGGCCA  
ACCCCTGGTCAGGGCAGAGGGAGTTGGGTGGGTGAGGCTCTGGGCTCACCTCCATCTCCAGA  
GCATCCCCTGCCTGCAGTTGTGGCAAGAACGCCAGCTCAGAATGAACACACCCCACCAAGA  
GCCTCCTTGTTCATAACCACAGGTTACCCCTACAAACCACTGTCCCCACACAACCTTGGGGAT  
GTTTTTAAACACACACCTCTAACGCATATCTTACAGTCACTGTTGTCTTGCCTGAGGGTTGA  
ATTTTTTTTAAATGAAAGTGCAATGAAAATCACTGGATTAAATCCTACGGACACAGAGCTGAA  
AAAAAAAAAAAAAAAAAAAAAAAAAAAAA

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## **FIGURE 188**

MNTWLLFLPLFPVQVQTLIVVIIGMLVLLDFLGLVHLGQLLI FHIYLSMSP TLSPRSPQGW

VVRAAHLTPLLEYVPNPEPPTPGARVFVPRVRMCSGSASPRSEIMDKKGKSQEEIKSMRTQQ

AQQEAELTPRPAGVVPGA



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FIGURE 189

GGAGTGCAGATGGCATCCTTCGGTTCTTCCAGACAAGCTGCAAGACGCTGACCAATGGCCAAG  
ATGGAGCTCTCGAAGGCCTTCTCTGGCCAGCGGACACTCCTATCTGCCATCCTCAGCATGCT  
ATCACTCAGCTTCTCCACAACATCCCTGCTCAGCAACTACTGGTTTGTGGGCACACAGAAGG  
TGCCCAAGCCCCCTGTGCGAGAAAAGGTCTGGCAGCCAAGTGCTTTGACATGCCAGTGTCCCTG  
GATGGAGATACCAACACATCCACCCAGGAGGTGGTACAATACAACCTGGGAGACTGGGGATGA  
CCGTTTCTCCTTCCGGAGCTTCCGGAGTGGCATGTGGCTATCCTGTGAGGAACTGTGGAAG  
AACCAGGGGAGAGGTGCCGAAGTTTCATTGAACTTACACCACCAGCCAAGAGAGGTGAGAAA  
GGACTACTGGAATTTGCCACGTTGCAAGGCCCATGTCACCCCACTCTCCGATTTGGAGGGAA  
GCGGTTGATGGAGAAGGCTTCCCTCCCCTCCCCTCCCCTGGGGCTTTGTGGCAAAAATCCTA  
TGGTTATCCCTGGGAACGCAGATCACCTACATCGGACTTCAATTCATCAGCTTCCTCCTGCT  
ACTAACAGACTTGCTACTCACTGGGAACCCCTGCCTGTGGGCTCAAACTGAGCGCCTTTGCTG  
CTGTTTCTCTGTCTCTGTCTCAGGTCTCCTGGGGATGGTGGCCCCACATGATGTATTCAACAAGTC  
TTCCAAGCGACTGTCAACTTGGGTCCAGAAGACTGGAGACCACATGTTTGGAATTATGGCTG  
GGCCTTCTACATGGCCTGGCTCTCCTTCACCTGCTGCATGGCGTCGGCTGTCACCACCTTCA  
ACACGTACACCAGGATGGTGCTGGAGTTCAAGTGCAAGCATAGTAAGAGCTTCAAGGAAAAC  
CCGAACTGCCTACCACATCACCATCAGTGTTCCTCGGCGGCTGTCAAGTGACGCCCCAC  
CGTGGGTCCTTTGACCAGCTACCACCAGTATCATAATCAGCCCATCCACTCTGTCTCTGAGG  
GAGTCGACTTCTACTCCGAGCTGCGGAACAAGGGATTTCAAAGAGGGGCCAGCCAGGAGCTG  
AAAGAAGCAGTTAGGTATCTGTAGAGGAAGAGCAGTGTTAGGAGTTAAGCGGGTTTGGGGA  
GTAGGCTTGAGCCCTACCTTACACGTCTGCTGATTATCAACATGTGCTTAAGCCAACATCCG  
TCTCTTGAGCATGGTTTTTAGAGGCTACGAATAAGGCTATGAATAAGGGTTATCTTTAAGTC  
CTAAGGGATTCTGGGTGCCACTGCTCTCTTTTCTCTACAGCTCCATCTGTTTCACCCAC  
CCCACATCTCACACATCCAGAATTCCTTCTTTACTGATAGTTTCTGTGCCAGGTCTGGGC  
TAAACCATGGAGATAAAAAGAAGAGTAAATACACTTCCCGACCTTAAGGATCTGAAA

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**FIGURE 190**

MAKMELSKAFSGQRTLLSAILSMLSLSFSTTSLLSNYWFVGTQKVPKPLCEKGLAAKCFDMP  
VSLDGD TNTSTQEVVQYNWETGDDRF SFRSFRSGMWLSCEETVEEPGERCRSFIELTPPAKR  
GEKGLLEFATLQGPCHPTLRFGGKRLMEKASLPSPPLGLCGKNPMVIPGNADHLHRTSIHQL  
PPATNRLATHWEPCLWAQTERLCCCFLCPVRS PGDGGPHDVFTSLP SDCQLGSRRL ETTCLE  
LWLGLLHGLALLHLLHGVGCHHLQH VHQDGAGVQVQA

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FIGURE 191

AACTGGAAGGAAAGAAAGAAAGGTCAGCTTTGGCCCAGATGTGGTTACCCCTTGGTCTCCTG  
TCTTTATGTCTTTCTCCTCTTCCTATTCTGTTCATCTCCCTCACTTAAGTCTCAGGCCTGTCA  
GCAGCTCCTGTGGACATTGCCATCCCCCTCTGGTAGCCTTCAGAGCAAAACAGGACAACCTATG  
TTATGGATGTTTCCACCAACCAGGGTAGTGGCATGGAGCACCGTAACCATCTGTGCTTCTGT  
GATCTCTATGACAGAGCCACTTCTCCACCTCTGAAATGTTCCCTGCTCTGAAATCTGGCATG  
AGATGGCACAGGTGACCACGCAGAAGCCACCAGAATCTTGCCCTGCCCTATTCCCTCCTCCCAA  
GTCTGTTCTCTTATTGTCAACCTCAGCACAAACAGGCTGGCGCCAATGGCATTACAGAGAAAAG  
CAATCTGTGTGGCTAGTGGGCAGATTACCATGCAAGCCCCAGGAGAAATGGAGGAGCTTTGT  
AGCCACCTCCCTGTCAGCCAGTATTAACATGTCCCCCTCCCCCTGCCCCGCGTAGATTTCAG  
GACATTCGCCCCCTGTGTGCCACCAAACCAGGACTTTCCCCCTTGGCTTGGCATCCCTGGCTCT  
CTCCTGGTACCCAGCAAGACGTCTGTTCCAGGGCAGTGTAGCATCTTTCAAGCTCCGTTACT  
ATGGCGATGGCCATGATGTTACAATCCCCTTGCCTGAATAATCAAGTGGGAAGGGGAAGCA  
GAGGGAAATGGGGCCATGTGAATGCAGCTGCTCTGTTCTCCCTACCCCTGAGGAAAAACCAA  
GGGAAGCAACAGGAACTTCTGCAACTGGTTTTTATCGGAAAGATCATCCTGCCTGCAGATGC  
TGTTGAAGGGGCACAAGAAATGTAGCTGGAGAAGATTGATGAAAGTGCAGGTGTGTAAGGAA  
ATAGAACAGTCTGCTGGGAGTCAGACCTGGAATTCTGATTCCAAACTCTTTATTACTTTGGG  
AAGTCACTCAGCCTCCCCGTAGCCATCTCCAGGGTGACGGAACCCAGTGTATTACCTGCTGG  
AACCAAGGAAACTAACAATGTAGGTTACTAGTGAATACCCCAATGGTTTCTCCAATTATGCC  
CATGCCACCAAAACAATAAAACAAAATTCTCTAACACTGAAA

**FIGURE 192**

MWLPLGLLSLCLSPLPILSSPSLKSQACQQLLWTLPSPLVAFRANRTTYVMDVSTNQSGME  
HRNRLCFCDLYDRATSPPLKCSLL

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FIGURE 193

GTAGCGCGTCTTGGGTCTCCCGGCTGCCGCTGCTGCCGCCGCCGCTCGGGTCGTGGAGCCA  
GGAGCGACGTCACCGCCATGGCAGGCATCAAAGC'TTGATTAGTTTGTCTTTGGAGGAGCA  
ATCGGACTGATGTTTTTATGCTTGGATGTGCCCTTCCAATATACAACAAATACTGGCCCT  
CTTTGTTCTATTTTTTACATCCTTTACCTATTCCATACTGCATAGCAAGAAGATTAGTGG  
ATGATACAGATGCTATGAGTAACGCTTGTAAGGAACCTGCCATCTTTCTTACAACGGGCATT  
GTCGTGTGAGCTTTTGGACTCCCTATTGTATTGTCAGAGCACATCTGATTGAGTGGGGAGC  
TTGTGCACTTGTCTCACAGGAAACACAGTCATCTTTGCAACTATACTAGGCTTTTTCTTGG  
TCTTTGGAAGCAATGACGACTTCAGCTGGCAGCAGTGGTGAAGAAATTAAGAACTATTG  
TCAAATGGACTTCCTGTCAATTTGTTGGCCATTACGCACACAGGAGATGGGGCAGTTAATGC  
TGAATGGTATAGCAAGCCTCTTGGGGGTATTTTAGGTGCTCCCTTCTCACTTTTATTGTAAG  
CATACTATTTTACAGAGACTTGCTGAAGGATTAAGGATTTTCTTTTGGAAAAGCTTG  
ACTGATTTTCACTTATCTATAGTATGCTTTTTTGTGGTGTCTGCTGAATTTAAATATTTAT  
GTGTTTTTCTGTTAGGTTGATTTTTTTTGAATCAATATGCAATGTTAAACACTTTTTTAA  
TGTAATCATTTGCATTGGTTAGGAATTCAGAATTCGCCGGCTCTATTACTGGTCAAGTACA  
TCTTTTCTCTTAAATATTTAGCCTCCATTATTACAAAAAATTATAAAAAATAAGTTTTTCA  
TCAGTCAGGATGACATCACTCCCAATGTTATGCAGACATACAGACGGTTGGCATACGTTATA  
GACTGTATACTCAGTGCAAATATAGCTGCATTTATACCTCAGAGGGGCCAAGTGTTAATGCC  
CATGCCCTCCGTTAAGGGTTGTTGGTTTTACTGGTAGACAGATGTTTTGTGGATTGAAAATT  
ATTTTATGGAATTGCTACAGAGGAGTGCTTTTCTCTCAATTGTTAGAAGAATTTATGTTAA  
ACTTTAAGGTAAGGGTGTAACAAACATTTTTGAGATAAGGTTTTTATTTATGTTTATTATTGT  
TAGAGTGAGTTGCAATGTGGGAAGAAATGACATTGAAATTCAGTTTTTGAATCCTGTTTCT  
ATTTATAAGTGAAATTTGTGATCTCCTATCAACCTTTTATGTTTTACCCTGTTAAATGGAC  
ATACATGGAACCACTACTGATGAGGGACAGTTGTATGTTGCATCATATATGCCAGAAAACC  
TTCTCTGCTTCTCTCTTTTGAATTTTGGTATGTTGTATATATTACATAAAATAACTTTT  
CAAATATAGTTTAAATAACACTTAGAAGTGTTTACTTACCTGGAAAATAATTGCTATGCCGTA  
CATTACAGAGTGCCCCCTCCCTGCAAGGCCTTGCCATGATTAACAAGTAACTTGTTAGTCTT  
ACAGATAATTCATGCATTAACAGTTTAAAGATTTAGACCATGGTAATAGTAGTTCCTTATTCTC  
TAAGGTTATATCATATGTAATTTAAAGTATTTTAAAGACAAGTTTCTGTATACCTCTGAA  
CTGTTTTGATTTTGAATTCATCATGATAGATCTGCTGTTTCTTATAAAAGGCATTTGTTGT  
GTGAGTTAATGCAAAGTAGCCAAGTCCAGCTATATAGCAGCTTCAGAAACATACCTGACCAA  
AAAATTTCCAGTAACCAGGCATGATCAATTTATAGTGGTCGTTTACATCTAATAATTATCAG  
GACTTTTTTTCAGGAGTGGGTATATAAAACATTCAAGTTGGTCTGACAGTATTTTGTAAAGGA  
TATTTGTTTGTATGTTTATTCAGTATACTTACATAAAATTTATTTGCCATCAGCCAAAAC  
CAGTAATCATGACAGCTGTCTGTTGTTTTATGAAGTTTATTTCTCAAGAAAATGGGAATAAA  
TTTGGGATTTGTTGAGCTTTTTTACTAAAGATGCCTAAAGCCACAGGTTTTATTGCCAACT  
TAAGCCATGACTTTTAGATATGAGATGACGGGAAGCAGGACGAAATATCGGCGTGTGGCTGG  
AGCCTTCCCACTGGAGGCTGAAAGTGGCTTGTGGTATTATAATGTTTCAAGAGGAA  
GGTGCAGGTACACATGAGTTAGAGAGCTGGTGAGACAGTTGGGAACCTTTTGTGCTTGTGAT  
CTACTGGACTTTTTTTTTTGCAGGAAGTGCAATTCCTGGTCCTTCCCTATTTTCTGTTCTGGA  
TGTCAGTGACAGTGCACTGCTACTGTTTTATCCACTTGGCCACAGACTTTTTTCTAACAGCTGC  
GTATTATTTCTATATACTAATTGCATTGGCAGCATTGTGTCTTTGACCTTGTATACTAGCTT  
GACATAGTGCTGTCTCTGATTTCTAGGCTAGTTACTTGAAGATATGAATTTTCCATAGAATAT  
GCACTGATACAACATTACCATTCTTCTATGGAAAGAAAACCTTTTGATGATGAAACAATAAAG  
ATTTTAAATATCTATTTTAAAAAATAA

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**FIGURE 194**

MAGIKALISLSFGGAIGLMFLMLGCALPIYNKYWPLFVLFFYILSPIPYCIARRLVDDTDAM  
SNACKELAIFLTGTGIVVSAFGLP1VFARAHLEWGACALVLTGNTVIFATILGFFLVFGSND  
DFSWQQW

## FIGURE 195A

CCACGCGTCCGCCACGCGTCCGCCACGCGTCCGCCACGCGTCCGCCACGCGTCCGCC  
CACGCGTCCGCCACGCGTCCGGTGCAGCTCGCGCCGCACACTGCCTGGTGGAGGAAGGA  
GCCCCGGCGCCTCTCGCGCTCCCGCGCCGCGCGTCCGCACCTCCCCACCGCCCGCGCCG  
CCGCGCGCGCCCGCAAGCATGAGTGAGCCCGCTCTCTGCAGTGCCTGCCGGGCGCAATGG  
CAGGCTGTTTTCCGCGGAGATAAAGGTGGCGCGGTAGTGGTCTGTTTCCAATGACGGACATT  
AACCAGACTGTGAGATCTTGGGGAGTTCGCGAGCCCCGAGTTTGGAGTTTTTTTCCCCCACA  
CGTCACAGTCCGAACTGCAGAGGGAAAGGAAGGCGGCAGGAAGGCGAAGCTCGGGCTCCGGC  
ACGTAGTTGGGAAACTTGGGGTCTAGAAGTGCCTCCCCGCTTGGCGCGCCCTTGCA  
GCCCGAGCCGAGCAGCAAAGTGAGACATTGTGCGCTGCCAGATCCGCGCGCGCGGACCG  
GGGCTGCCTCGGAAACACAGAGGGGTCTTCTCTCGCCCTGCATATAATTAGCCTGCACACA  
AGGGAGCAGCTGAATGGAGGTTGTCACTCTCTGAAAAGGATTCTGACCGAGCGCTTCCAT  
TGGACATTCTCCAGTCTCTCTGAAAAGATTCTCGTAATTGGATTCTTGCTGCTCGGTCTCT  
GTCTATACCTGGCTGCTGAGGAGCCCTCGGGGTGGTCTTGTTGTCTGCTGGGGCTGCTTT  
GATAGTCTGCCCGCGCCCCCGCGGGTGCCTGCGAGCTGTGCGGGTGCAGGGGCGGTGCT  
CTACTGCGAGGCGCTCAACCTCACCGAGGCGCCCCACAACCTGTCCGGCTGCTGGGCTTGT  
CCCTGCGCTACAACAGCCTCTCGGAGCTGCGCGCGCGCCAGTTCACGGGGTTAATGCAGCTC  
ACGTGGCTCTATCTGGATCACAATCACATCTGCTCCGTGCAGGGGGACGCTTTCAGAACT  
GCGCCGAGTTAAGAACTCAGCTGAGTTTCAACACAGTACCCAACTGCCAACACCACT  
TCCGCCCCATGCCAACCTGCGCAGCGTGGACCTCTCGTACAACAAGCTCGAGGCGCTCGCG  
CCCGACCTCTTCCACGGGTGCGGAAGCTCACCACGCTGCATATGCGGGCCAAACGCCATCCA  
GTTTTGTGCCCGTGCAGCATCTTCCAGGACTGCGCGAGCCTCAAGTTTCTCGACATCGGATACA  
ATCAGCTCAAGAGCTTGGCGCGCAACTCTTTCGCGGCTGTTTTAAGCTCACCAGAGCTGCAC  
CTCGAGTCAACAGTCTGGTCAAGGTGAATCTGCGCCACTTCCGCGCTCATCTCCCTGCA  
CTCGCTCTGCTGCGGAGGAACAAGGTGGCCATTGTGGTCACTGCTGGAAGTGGGTTTGA  
ACCTGGAGAAAATGGACTTGTGCGGCAACGAGATCGAGTACATGGAGCCCCATGTGTTGAG  
ACCGTGCCGCACTTGAGTCCCTGCAGCTGGACTCCAACCGCTCACCTACATCGAGCCCCG  
GATCTCACTCTTGAAGTCCCTGACAAGCATCACCTGGCGGGAACTGTGGGATTGCG  
GGCGCAACGCTGTGTGCCCTAGCCTCGTGGCTCAGCAACTTCCAGGGGCGCTACGATGGCAAC  
TTGCACTGCGCCAGCCCGAGTACGCACAGGGCGAGGACGCTCTGGACGCGGTGTACGCCCT  
CCACCTGTGCGAGGATGGGGCCGAGCCCAACGCGGCCACCTGCTCTCGGCCGTACCAAC  
GCAGTGATCTGGGGCCCCCTGCCAGCTCGGCCACCAAGCTCGGCGAGCGGGAGGGGAG  
CAGCAGCGGCATCTGAGCCTGCCACCGTGGCTCTTCCAGGCGCGAGCAGCCGAGAACGC  
CGTGCAATCCACAAGGTGGTACGGGCAACATGGCCCTCATCTTCTCCTTCTCATCTGTTG  
TCCTGGTGTCTTACGTGTCTGGAAGTGTTCACAGCCAGCCTCAGGCACTCAGACAGTGC  
TTTGTTCAGCAGCGCAGGAAGCAAAAGCAGAAACAGCACTCATGATGGCTGCCATGTCT  
TGCCAGGAATACTACGTTGATTACAACCGAACCATGAGGGAGCCCTGGTGTATCATCA  
ACGAGTATGGCTCGTGTACCTGCCACCAGCAGCCCGCGAGGGAATGCGAGGTGTGATTGTCC  
CAGTGGCTCTCAACCCATGCGCTACCAATACGCTGGGCGAGCCGGGACGGGCGCGCGGCA  
CCAGGCTGGGGTCTCCTTGTCTGTGCTCTGATATGCTCCTTGACTGAACTTTAAGGGGATC  
TCTCCAGAGACTTGACATTTTAGCTTTATTGTGCTTTAAAAACAAAAGCGAATTAACAC  
AACAAAAAACCCCAACCAACCTTCAAGCAGTCTATCTTAAATTTTATATGAGAATCC  
TTCTCCTTTTGAAGATCTGTCCATATTAGGAATCTGAGAGTGTAAAAAAGGTGGCCATAA  
GACAGAGAGAGAATAATCGTGCTTTGTTTTATGCTACTCCTCCACCTTGCCCATGATTAA  
CATCATGTATGTAGAAGATCTTAAGTCCATACGCATTTTATGAAGAACCTTGAAGAGGA  
ATCTGCAATCTGGGAGCTTAAGAGCAATGATGACCATGAAAGCTATGTTCTTACTTTGTG  
TGTGTGTCTGTATGTTTCTGCGTGTGTGTCTTTGTAGGAGCAACGCTTGTCTACACAA  
CGGGAATTTAGCTCACATATTTTATGCCCCGTGTCCTCTAGCTCTGGAGATTGGTGGGGG  
AGGTGGGGGGAACCGGAGGAATAAGGGAAAGTGTAAGTTTAACTAAGGTTTTGTAACTC  
TGAATCTTTTCTTTCTCAAATTAATTTAAGCTTTCAAGAACTTGCTCTGACCCCT  
TAAGCAAACTACTAAGCATTTAAAGAGAATACTAATTTTAAAGGTGTAGCACCTTTTTTT  
TATTCTTCCACAGAGGGTGTAACTCTCATTATGCTGTGCTATCTGAAAAGAACTTAAGGCC  
ACAATTACGCTCTCGTCTGGGCTATTGTGATGGATTGACCTTCCATTGTCAGTACCTTCCCA  
GCTGATTAAAGTTAGCAGTGGTATTGAGGTTTTTCAATATTTATAGAAAAAAGTCTT  
TTCCAGATGACAAATGACACTCTCACACGAGCTTAGCCCTAGTAGTTTTTTAGGTTGGACCA  
GAGGAAGCAGGTTAAATGAGACCTGTCTCTGCACTCAGAAAAAATAGGCAGTCCCTGA  
TGCTCAGATCTTAGCCTTGATATTAATAGTTGAGACCACCTACCCACAATGCAGCCTATAC  
CCCAAGACTACAAAGTTACCATCGCAAGGAAAGGTTATTCCAGTAAAAGGAAATAGTTTCT  
CTAACCATTTAAAAATATTCTTGAATCATCAAAGTAGAAGAGCCCCAACCTTTTCTCT  
TGCCCTTCAAGAAAGGCAGACATTTGGTATGATTTAGCATCAACAACATTTATGATATAT

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FIGURE 195B

GTAAGTAATCAGAGGGGCAAATGCCACTTGTTATTCCTCCCAAGTTTTCCAAGCAAGTACAC  
ACAGATCTCTGGTAGGATTAGGGGCCACTTGTTGTTTCCGGCTTATTTTAGTCGACTTGTGAG  
CAAGTTTGATGCCTAGTCTATCTGACATGGCCCAGTAGAACAGGGCATTGATGGATCACATG  
AGATGGTAGAAGGAACATCATCACATACCCCTCTCACAGAGAAAATTATCAAAGAACCAGAA  
ATTATATCTGTTTTGGAGCAAGAGTGTCTATAATGTTTCAGGGTAGTCAAAATAAACATAAAT  
TATCTCCTCTAGATGAGTGGCGATGTTGGCTGATTTGGGTCTGCCATTGACAGAATGTCAAA  
TAAAAAGGAATTAGCTAGAATATGACCATTAAATGTGCTTCTGAAATATATTTTGAGATAGG  
TTTAGAATGTCA



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FIGURE 196

MDFLLLGLCLYWLLRRPSGVVLCLLGACFQMLPAAPSGCPQLCRCEGRLLYCEALNLTEAPH  
NLSGLLGLSLRYNSLSELRAGQFTGLMQLTWLYLDHNIHICSVQGDAFQKLRRVKELTLSSNQ  
ITQLPNTTFRPMPNLRSDLSYNKLQALAPDLFHGLRKLTTLHMRANAIQFVPVRIFQDCRS  
LKFLDIGYNQLKSLARNSFAGLFKLTEHLEHNDLVKVNFAHFPRLISLHSLCLRRNKVAIV  
VSSLDWVWNLEKMDLSGNEIEYMEPHVFETVPHLQSLQLDSNRLTYIEPRILNSWKSLSIT  
LAGNLWDCGRNVCALASWLSNFQGRYDGNLQCASPEYAQGEDVLDVYAFHLCEDGAEPTSG  
HLLSAVTNRSDLGPPASSATTADGGEGQHDGTFEPATVALPGGEHAENAVQIHKVVTGTMA  
LIFSFLIVVLVLYVSWKCFPASLRQLRQCFVTQRRKQKQKQTMHQAAMSAQEYYVDYKPNH  
IEGALVIINEYGSCTCHQQPARECEV

FIGURE 197

GTGCAAGGAGCCGAGGCGAGATGGGCGTCCTGGGCCGGGTCCCTGCTGTGGCTGCAGCTCTGC  
GCACTGACCCAGGCGGTCTCCAACTCTGGGTCCCCAACACGGACTTCGACGTCGCAGCCAA  
CTGGAGCCAGAACCGGACCCCGTGCGCCGGCGGCGCCGTTGAGTTCCCGGCGGACAAGATGG  
TGTCAGTCCTGGTGCAAGAAGGTCACGCCGTCTCAGACATGCTCCTGCCGCTGGATGGGGAA  
CTCGTCCTGGCTTCAGGAGCCGGATTGGGCGTCTCAGACGTGGGCTCGCACCTGGACTGTGG  
CGCGGGCGAACCTGCCGTCTTCGCGACTCTGACCGCTTCTCCTGGCATGACCCGCACCTGT  
GGCGCTCTGGGGACGAGGCACCTGGCCTCTTCTTCGTGGACGCCGAGCGCGTGCCCTGCCGC  
CACGACGACGTCTTCTTTCCGCCTAGTGCCTCCTTCGCGTGGGGCTCGGCCCTGGCGCTAG  
CCCCGTGCGTGTCCGCAGCATCTCGGCTCTGGGCCGGACGTTACGCGCGACGAGGACCTGG  
CTGTTTTCTGGCGTCCCGCGCGGGCCGCCTACGCTTCCACGGGCCGGGCGCGCTGAGCGTG  
GGCCCCGAGGACTGCGCGGACCCGTGGGCTGCGTCTGCGGCAACGCGGAGGCGCAGCCGTG  
GATCTGCGCGGCCCTGCTCCAGCCCCT

FIGURE 198

MGVLGRVLLWLQLCALTQAVSKLWVPNTDFDVAANWSQNRTPCAGGAVEFPADKMVSVLVQE  
GHAVSDMLLPDGLVVLASGAGFGVSDVGSHLDGAGEPAVFRDSDRFSWHDPHLWRSIDEA  
PGLFFVDAERVPCRHDDVFFPPSASFVGLGPGASPVVRVRSISALGRFTTRDEDLAVFLASR  
AGRRLRFHGPALSVGPEDCADPSGCVCGNAEAQFWICAALLQP

[illegible]

FIGURE 200

MGPVKQLKRMFEPTRLIATIMVLLCFALTLCSAFWWHNKGLALIFCILQSLALTWYSLSFIP  
FARDAVKKCFVCLA

FIGURE 201

TTGAGCGCAGGTGAGCTCCTGCGCGTTCCGGGGGCGTTCTCCAGTCACCCTCCCGCCGTTA  
CCCGCGGCGCGCCCGAGGGAGTCTCTCCAGACCCTCCCTCCCGTTGCTCCAACTAATACG  
GACTGAACGGATCGCTGCGAGGGTGGGAGAGAAAATTAGGGGGAGAAAGGACAGAGAGAGCA  
ACTACCATCCATAGCCAGATAGATTATCTTACACTGAACTGATCAAGTACTTTGAAAATGAC  
TTCGAAATTTATCTTGGTGTCTTCATACTTGCTGCACTGAGTCTTCAACCACCTTTTCTC  
TCCAAC TAGACCAGCAAAAGGTTCTACTAGTTTCTTTTGATGGATTCCGTTGGGATTACTTA  
TATAAAGTTCCAACGCCCCATTTTCATTATATTTATGAAATATGGTGTTACAGTGAAGCAAGT  
TACTAATGTTTTATTACAAAACCTACCCTAACCATTTACTTTGGTAACTGGCCTCTTTG  
CAGAGAATCATGGGATTGTTGCAAATGATATGTTTGATCCTATTTCGGAACAAATCTTTCTCC  
TTGGATCACATGAATATTTATGATTCCAAGTTTTGGGAAGAAGCGACACCAATATGGATCAC  
AAACCAGAGGGCAGGACATACTAGTGGTGCAGCCATGTGGCCCGGAACAGATGTAAAATAC  
ATAAGCGCTTTCTACTCATTACATGCCTTACAATGAGTCAGTTTCATTTGAAGATAGAGTT  
GCCAAAATGTTGAATGGTTTTACGTCAAAGAGCCCATAAATCTTGGTCTTCTCTATTGGGA  
AGACCCTGATGACATGGGCCACCATTGGGACCTGACAGTCCGCTCATGGGGCCTGTCATTT  
CAGATATTGACAAGAAGTTAGGATATCTCATACAAATGCTGAAAAAGGCAAAGTTGTGGAAC  
ACTCTGAACCTAATCATCACAAGTGATCATGGAATGACGCAGTGCTCTGAGGAAAGGTTAAT  
AGAACTTGACCAGTACCTGGATAAAGACCACTATACCCTGATTGATCAATCTCCAGTAGCAG  
CCATCTTGCCAAAAGAAGGTAAATTTGATGAAGTCTATGAAGCACTAACTCACGCTCATCCT  
AATCTTACTGTTTACAAAAAAGAAGACGTTCCAGAAAGGTGGCATTACAAATACAACAGTCG  
AATTCAACCAATCATAGCAGTGGCTGATGAAGGGTGGCACATTTTACAGAATAAGTCAGATG  
ACTTTCTGTTAGGCAACCACGGTTACGATAATGCGTTAGCAGATATGCATCCAATAATTTTA  
GCCCATGGTCTGCTTCAGAAAGAAATTTCTCAAAGAGCCATGAACTCCACAGATTTGTA  
CCCCTACTATGCCACCTCCTCAATATCACTGCCATGCCACACAATGGATCATTCTGGAATG  
TCCAGGATCTGCTCAATTCAGCAATGCCAAGGGTGGTCCCTTATACACAGAGTACTATACTC  
CTCCCTGGTAGTGTTAAACCAGCAGAATATGACCAAGAGGGGTCATACCCTTATTTTCATAGG  
GGTCTCTCTTGGCAGCATTATAGTGATTGTATTTTTTGTAAATTTTCATTAAGCATTTAATTC  
ACAGTCAAATACCTGCCTTACAAGATATGCATGCTGAAATAGCTCAACCATTATTACAAGCC  
TAATGTTACTTTGAAGTGGATTTGCATATTGAAGTGGAGATTCCATAATTATGTCAGTGTTT  
AAAGGTTTTCAAATTTCTGGGAAACAGTTCCAAACATCTGCAGAAACCATTAAGCAGTTACAT  
ATTTAGGTATACACACACACACACACACATACACACACACGACCAAAATACTTACAC  
CTGCAAAGGAATAAAGATGTGAGAGTATGTCTCCATTGTTCACTGTAGCATAGGGATAGATA  
AGATCCTGCTTTATTTGGACTTGGCGCAGATAATGTATATATTTAGCAACTTTGCACTATGT  
AAAGTACCTTATATATTGCATTTTAAATTTCTCTCCTGATGGGTACTTTAATTTGAAATGCA  
CTTTATGGACAGTTATGTCTTATAACTTGATTGAAAATGACAACTTTTTGCACCCATGTAC  
AGAATACTTGTTACGCATTGTTCAAACCTGAAGGAAATTTCTAATAATCCCGAATAATGAACA  
TAGAAATCTATCTCCATAAATTGAGAGAAGAAGAAGGTGATAAGTGTTGAAAATTTAAATGTG  
ATAACCTTTGAACCTTGAAATTTTGAGATGTATTCCCAACAGCAGAATGCAACTGTGGGCAT  
TTCTTGCTTATTTCTTTCCAGAGAACGTGGTTTTTCATTTATTTTTCCCTCAAAGAGAGTC  
AAATACTGACAGATTCGTTCTAAATATATTGTTTCTGTCTATAAAATTAATTGTGATTTCTGTA  
TGAGTCATATTACTGTGATTTTCTAATAATGAAGACACCATGAATATACTTTTCTCTATA  
TAGTTTCAGCAATGGCCTGAATAGAAGCAACCAGGCACCATCTCAGCAATGTTTTCTCTGTT  
TGTAATTAATTTGCTCCTTTGAAAATTAATCACTATTAATTACATTAATAATCAAATTGGAT  
AAAAAAAAAAAAAAAAAAAA

FIGURE 202

MTSKFILVSFILAALSLSTTFSLQLDQQKVLLVSFDGFRWDYLYKVPTPHFHYIMKYGVHVK  
QVTNVFITKTYPNHYTLVTGLFAENHGIVANDMFDPIRNKSFSLDHMNIYDSKFWEEATPIW  
ITNQRAGHTSGAAMWPGTDVKIHKRFPTHYMPYNESVSFEDRVAKIVEWFTSKEPINLGLLY  
WEDPDDMGHHLGPDSPLMGPVISDIDKKLGYLIQMLKKAKLWNTLNLIITSDHGMTQCSEER  
LIELDQYLDKDHYYTLIDQSPVAAILPKEGKFDEVYEALTHAHPNLTVYKKEDVPERWHYKYN  
SRIQPIIAVADEGWHILQNKSDDFLLGNHGYDNALADMHPIFLAHGPAFRKNFSKEAMNSTD  
LYPLLCHLLNITAMPHNGSFWNVQDLLNSAMPRVVPYTQSTILLPGSVKPAEYDQEGSYPYF  
IGVSLGSIIVIVFFVIFIKHLIHSQIPALQDMHAEIAQPLLQA

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FIGURE 203

GGATTTTTGTGATCCGCGATTGCTCCCACGGGCGGGACCTTTGTAAGTCCGGGAGGCCCAG  
GACAGGCCCCACCCTGCGGGGCGGGAGGCAGCCGGGGTGAGGGAGGTGAAGAAACCAAGACGC  
AGAGAGGCCAAGCCCCCTTGCTTGGGTACACAGCCAAAGGAGGCAGAGCCAGAACTCACAA  
CCAGATCCAGAGGCAACAGGGACATGGCCACCTGGGACGAAAAGGCAGTCACCCGCAGGGCC  
AAGGTGGCTCCCGCTGAGAGGATGAGCAAGTTCTTAAGGCACTTCACGGTCGTGGGAGACGA  
CTACCATGCCTGGAACATCAACTACAAGAAATGGGAGAATGAAGAGGAGGAGGAGGAGG  
AGCAGCCACCACCCACACCAGTCTCAGGCGAGGAAGGCAGAGCTGCAGCCCCCTGACGTTGCC  
CCTGCCCCCTGGCCCCGCACCCAGGGCCCCCCTTGACTTCAGGGGCATGTTGAGGAACTGTT  
CAGCTCCACAGGTTTCAGGTCATCATCATCTGCTTGGTGGTTCTGGATGCCCTCCTGGTGC  
TTGCTGAGCTCATCCTGGACCTGAAGATCATCCAGCCCGACAAGAATAACTATGCTGCCATG  
GTATTCACCTACATGAGCATCACCATCTTGGTCTTTTTTATGATGGAGATCATCTTTAAATT  
ATTTGCTCTCCGCCTGAGTTCTTTCACCACAAGTTTGAGATCCTGGATGCCCGTCGTGGTGG  
TGGTCTCATTCATCCTGGACATTGTCCTCCTGTTCCAGGAGCACCAGTTTGAGGCTCTGGGC  
CTGCTGATTCTGCTCCGGCTGTGGCGGGTGGCCCGGATCATCAATGGGATTATCATCTCAGT  
TAAGACACGTTCAGAACGGCAACTCTTAAGGTTAAACAGATGAATGTACAATTGGCCGCCA  
AGATTCAACACCTTGAGTTCAGCTGCTCTGAGAAGCCCCCTGGACTGATGAGTTTGCTGTATC  
AACCTGTAAGGAGAAGCTCTCTCCGGATGGCTATGGGAATGAAAGAATCCGACTTCTACTCT  
CACACAGCCACCGTGAAAGTCCTGGAGTAAATGTGCTGTGTACAGAAGAGAGAGAAGGAAG  
CAGGCTGGCATGTTCACTGGGCTGGTGTACGACAGAGAACCTGACAGTCACTGGCCAGTTA  
TCACTTCAGATTACAAATCACACAGAGCATCTGCCTGTTTTCAATCACAAGAGAACAAAACC  
AAAATCTATAAAGATATTCTGAAAATATGACAGAATTTGACAAATAAAAGCATAAACGTGTA  
AAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAA



FIGURE 204

MATWDEKAVTRRAKVAPAERMSKFLRHFTVVGDDYHAWNINYKKWENEEEEEEQPPPTPV  
SGEEGRAAAPDVAPAPGPAPRAPLDFRGLRKLFSHRFQVIIICLVVLDALLVLAELIDL  
KIIQPDKNNYAAMVFHYMSITILVFFMMEIIFKLFVFRLLSSFTTSLRSWMPVVVVVSFILD  
VLLFQEHQFEALGLLILLRLWRVARIINGIIISVKTRSERQLRLKQMNVLAAKIQHLEFS  
CSEKPLD



FIGURE 206

MLCLCLYVPVIGEAQTEFQYFESKGLPAELKSIFKLSVFIPSQEFSTYRQWKQKIVQAGDKD  
LDGQLDFEEFVHYLQDHEKKLRLVFKILDKKNDGRIDAQEQIMQSLRDLGVKISEQQAEEKILK  
SMDKNGTMTIDWNEWRDYHLLHPVENIPEIILYWKHSTIFDVGENLTPDEFTVEERQTGMW  
WRHLVAGGGAGAVSRTCTAPLDRKVLMOVHASRSNNMGIVGGFTQMIREGGARSLWRGNGI  
NVLKIAPESAIKFMAYEQIKRLVGSDQETLRIHERLVAGSLAGAIQSSIYPMEVLKTRMAL  
RKTGQYSGMLDCARRILAREGVAAFYKGYVPNMLGIIPYAGIDLAVYETLKNAWLQHYAVNS  
ADPGVFVLLACGTMSSTCGQLASYPLALVRTRMQAQASIEGAPEVTMSSLFKHILRTEGAFG  
LYRGLAPNFMKVIPAVSISYVVYENLKITLGVQSR

FIGURE 207

[illegible]

FIGURE 208

MASLGQILFWSIISIIIIILAGATAIIIGFGISGRHSITVTTVASAGNIGEDGILSCTFEPDI  
KLSDIVIQWLKEGVLGLVHEFKEGKDELSEQDEMFRGRTAVFADQVIVGNASLRLKNVQLTD  
AGTYKCYIITSKGKGNANLEYKTGAFSMPEVNVVDYNASSETLRCEAPRWFPPQPTVVWASQVD  
QGANFSEVSNTSFELNSENVTMKVVSVLNVNTINNTYSCMIENDIAKATGDIKVTSESEIKRR  
SHLQLLNSKASLCVSSFFAISWALLPLSPYMLK

FIGURE 209

[illegible]

FIGURE 210

MAASLGQVLALVLVAALWGGTQPLLKRASAGLQRVHEPTWAQQLQEMKTLFLNTEYLMPFL  
LNQCGSLLYYLTLASTDLTLAVPICNSLAIFTLIVGKALGEDIGGKRKLDYCECGTQLCGS  
RHTCVSSFPEPISPEWVRTRPFPILPFPLQLFCFLVAIRVPFPWTVWRKTEAGVWD

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FIGURE 211

CTTCTGTAGGACAGTCACCAGGCCAGATCCAGAAGCCTCTCTAGGCTCCAGCTTTCTCTGTG  
GAAGATGACAGCAATTATAGCAGGACCCTGCCAGGCTGTCGAAAAGATTCCGCAATAAACT  
TTGCCAGTGGGAAGTACCTAGTGAAACGGCCTAAGATGCCACTTCTTCTCATGTCCCAGGCT  
TGAGGCCCTGTGGTCCCCATCCTTGGGAGAAGTCAGCTCCAGCACCATGAAGGGCATCCTCG  
TTGCTGGTATCACTGCAGTGCTTGTTCAGCTGTAGAATCTCTGAGCTGCGTGCAAGTGAAT  
TCATGGGAAAAATCCTGTGTCAACAGCATTGCCCTCTGAATGTCCCTCACATGCCAACACCAG  
CTGTATCAGCTCCTCAGCCAGCTCCTCTCTAGAGACACCAGTCAGATTATACCAGAATATGT  
TCTGCTCAGCGGAGAACTGCAGTGAGGAGACACACATTACAGCCTTCACTGTCCACGTGTCT  
GCTGAAGAACACTTTTCATTTTGTAAAGCCAGTGCTGCCAAGGAAAGGAATGCAGCAACACCAG  
CGATGCCCTGGACCCCTCCCCTGAAGAACGTGTCCAGCAACGCAGAGTGCCCTGCTTGTATG  
AATCTAATGGAACTTCCTGTGCTGGGAAGCCCTGGAAATGCTATGAAGAAGAACAGTGTGTC  
TTTCTAGTTGCAGAACTTAAGAATGACATTGAGTCTAAGAGTCTCGTGCTGAAAGGCTGTTT  
CAACGTCAGTAACGCCACCTGTCAAGTTCCTGTCTGGTGAAAACAAGACTCTTGGAGGAGTCA  
TCTTTTCGAAAGTTTGAAGTGTGCAAATGTAAACAGCTTAACCCCCACGTCTGCACCAACCACT  
TCCCACAACGTGGGCTCCAAAGCTTCCCTCTACCTCTTGGCCCTTGCCAGCCTCCTTCTTCG  
GGGACTGCTGCCCTGAGGTCCCTGGGGCTGCACTTTGCCCAGCACCCCATTTCTGCTTCTCTG  
AGGTCCAGAGCACCCCCTGCGGTGCTGACACCCTCTTCCCTGCTCTGCCCCGTTTAACTGC  
CCAGTAAGTGGGAGTCACAGGTCTCCAGGCAATGCCGACAGCTGCCTTGTTCTTCATTATTA  
AAGCACTGGTTCACTTCACTGCCAAAAAAAAAAAAAAAAAAAAAAAAAAAAA



FIGURE 212

MKGILVAGITAVLVAAVESLSCVQCNSWEKSCVNSIASECPSHANTSCISSSASSSLETPVR  
LYQNMFCSAENCSEETHITAFTVHVSAEEHFHFVSQCCQGKECSNTSDALDPPLKNVSSNAE  
CPACYESNGTSCRGKPWKCYEEEQCVFLVAELKNDIESKSLVLKGCSNVSNATCQFLSGENK  
TLGGVIFRKFECANVNSLTPTSAPTTSNVGSKASLYLLALASLLLRGLLP

FIGURE 213

GGCCTCGGTTCAAACGACCCGGTGGGTCTACAGCGGAAGGGAGGGAGCGAAGGTAGGAGGCA  
GGGCTTGCCTCACTGGCCACCCTCCCAACCCCAAGAGCCCAGCCCCAATGGTCCCCGCCGCCG  
GCGCGCTGCTGTGGGTCTGCTGCTGAATCTGGGTCCCCGGGCGGCGGGGGCCCAAGGCCTG  
ACCCAGACTCCGACCGAAATGCAGCGGTGAGTTTACGCTTTGGGGCCCCATGACCCGCAG  
CTACCGGAGCACCGCCCGGACTGGTCTTCCCCGGAAGACAAGGATAATCCTAGAGGACGAGA  
ATGATGCCATGGCCGACGCCGACCGCCTGGCTGGACCAGCGGCTGCCGAGCTCTTGCCGCC  
ACGGTGTCCACCGGCTTTAGCCGGTCGTCCGCCATTAACGAGGAGGATGGGTCTTCAGAAGA  
GGGGTTGTGATTAATGCCGGAAGGATAGCACCAGCAGAGAGCTTCCAGTGCGACTCCCA  
ATACAGCGGGAGTTCCAGCACGAGGTTTATAGCCAATAGTCAGGAGCCTGAAATCAGGCTG  
ACTTCAAGCCTGCCGCGCTCCCCGGGAGGTCTACTGAGGACCTGCCAGGCTCGCAGGCCAC  
CCTGAGCCAGTGGTCCACACCTGGGTCTACCCGAGCCGGTGGCCGTACCCCTACCCACAG  
CCATGCCATCTCCTGAGGATCTGCGGCTGGTGCTGATGCCCTGGGGCCCGTGGCACTGCCAC  
TGCAAGTCGGGCACCATGAGCCGGAGCCGGTCTGGGAAGCTGCACGGCCTTTCCGGGCGCCT  
TCGAGTTGGGGCGCTGAGCCAGCTCCGCACGGAGCACAAGCCTTGACCTATCAACAATGTC  
CCTGCAACCGACTTCGGGAAGAGTGCCCCCTGGACACAAGTCTCTGTACTGACACCAACTGT  
GCCTCTCAGAGCACCAAGTACCAGGACCACCACTACCCCTTCCCCACCATCCACCTCAG  
AAGCAGTCCCAGCCTGCCACCCGCCAGCCCCTGCCAGCCCTGGCTTTTGGAAACGGGTCA  
GGATTGGCCTGGAGGATATTTGGAATAGCCTCTCTTCAGTGTTACAGAGATGCAACCAATA  
GACAGAAACCAGAGGTAATGGCCACTTCATCCACATGAGGAGATGTCAGTATCTCAACCTCT  
CTTGCCCTTTCAATCCTAGCACCCACTAGATATTTTTAGTACAGAAAAACAAACTGGAAAA  
CACAA

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FIGURE 214

MVPAAGALLWVLLLNIGPRAAGAQGLTQTPTEMQRVSLRFGGPMTRSYRSTARTGLPRKTRI  
ILEDENDAMADADRLAGPAAAEELLAATVSTGFSRSSAINEDGSSEEGVVINAGKDSTSREL  
PSATPNTAGSSSTRFIANSQEPEIRLTSSLPRSPGRSTEDLPGSQATLSQWSTPGSTPSRWF  
SPSPTAMPSPEDLRLVLMWPWGPWHCHCKSGTMSRSRSGKLHGLSGRLRVGALSQLRTEHKPC  
TYQQCPCNRLREECPLDTSLCDTNCASQSTTSTRTTTTPFPTIHLRSSPSLPPASPCPALA  
FWKRVIRIGLEDIWNLSLSSVFTEMQPIDRNQR

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FIGURE 215

CCCCGGTTCGACCCACGCGTCCGGGGAGAAAGGATGGCCGGCCTGGCGGCGCGGTGGTTCCTG  
CTAGCTGGGGCAGCGGCGCTGGCGAGCGGCTCCCAGGGCGACCGTGAGCCGGTGTACCGCGA  
CTGCGTACTGCAGTGCAGAGCAGAACTGCTCTGGGGGCGCTCTGAATCACTTCCGCTCCC  
GCCAGCCAATCTACATGAGTCTAGCAGGCTGGACCTGTGGGACGACTGTAAGTATGAGTGT  
ATGTGGGTACCGTTGGGCTCTACCTCCAGGAAGGTCACAAAGTGCCTCAGTTCCATGGCAA  
GTGGCCCTTCTCCCGGTTCTGTCTTTCAAGAGCCGGCATCGGCCGTGGCCTCGTTTCTCA  
ATGGCCTGGCCAGCCTGGTGATGCTCTGCCGCTACCGCACCTTCGTGCCAGCCTCCTCCCC  
ATGTACCACACCTGTGTGGCCTTCGCCTGGGTGTCCCTCAATGCATGGTTCTGGTCCACAGT  
CTTCCACACCAGGGACACTGACCTCACAGAGAAAATGGACTACTTCTGTGCCTCCACTGTCA  
TCCTACACTCAATCTACCTGTGTGCTGCGTCAGGACCGTGGGGCTGCAGCACCCAGCTGTGGTC  
AGTGCCTTCCGGGCTCTCCTGCTGCTCATGCTGACCGTGACGTCTCCTACCTGAGCCTCAT  
CCGCTTCGACTATGGCTACAACCTGGTGGCCAACGTGGCTATTGGCCTGGTCAACGTGGTGT  
GGTGGCTGGCCTGGTGCTGTGGAACCAGCGGCGCTGCCTCACGTGCGCAAGTGCGTGGTG  
GTGGTCTTGCTGCTGCAGGGGCTGTCCCTGCTCGAGCTGCTTGACTTCCACCGCTCTTCTG  
GGTCTGGATGCCCATGCCATCTGGCACATCAGCACCATCCCTGTCCACGTCTCTTTTCA  
GCTTCTGGAAGATGACAGCCTGTACCTGCTGAAGGAATCAGAGGACAAGTTCAAGCTGGAC  
**TGA**AGACCTTGAGCGAGTCTGCCCCAGTGGGGATCCTGCCCCGCGCCTGCTGGCCTCCCTT  
CTCCCCCTCAACCTTGAGATGATTTTCTCTTTTCAACTTCTTGAACCTGGACATGAAGGATG  
TGGGCCCAGAATCATGTGGCCAGCCCACCCCTGTTGGCCCTCACCAGCCTTGAGTCTGTT  
CTAGGGAAGGCCTCCAGCATCTGGGACTCGAGAGTGGGAGCCCTCTACCTCCTGGAGCT  
GAACTGGGGTGAACTGAGTGTGTTCTTAGCTCTACCGGAGGACAGCTGCCTGTTTCTCTCC  
CCACCAGCCTCCTCCCCACATCCCCAGCTGCCTGGCTGGGTCTCTGAAGCCCTCTGTCTACCT  
GGGAGACCAGGGACCACAGGCCTTAGGGATACAGGGGGTCCCCCTCTGTTTACACCCCCAC  
CCTCCTCCAGGACACCACTAGGTGGTGTGATGCTTGTCTTTGGCCAGCCAAGGTTACG  
GCGATTCTCCCATGGGATCTTGAGGGACCAAGCTGCTGGGATTGGGAAGGAGTTTACCCCT  
GACCGTTGCCCTAGCCAGGTTCCAGGAGGCCTCACCATACTCCCTTTCAGGGCCAGGGCTC  
CAGCAAGCCCAGGGCAAGGATCCTGTGCTGCTGTCTGGTTGAGAGCCTGCCACCGTGTGTG  
GGAGTGTGGGCCAGGCTGAGTGCATAGGTGACAGGGCCGTGAGCATGGGCCTGGGTGTGTG  
GAGCTCAGGCCTAGGTGCGCAGTGTGGAGACGGGTGTTGTGCGGGGAAGAGGTGTGGCTTCAA  
AGTGTGTGTGTGCAGGGGGTGGGTGTGTAGCGTGGGTAGGGGAACGTGTGTGCGCGTGTG  
GGTGGGCATGTGAGATGAGTGACTGCCGCTGAATGTGTCCACAGTTGAGAGGTTGGAGCAGG  
ATGAGGGAATCCTGTCACCATCAATAATCACTTGTGGAGCGCCAGCTCTGCCCCAAGACGCCA  
CCTGGGCGGACAGCCAGGAGCTCTCCATGGCCAGGCTGCCTGTGTGCATGTTCCCTGTCTGG  
TGCCCCCTTGGCCGCTCCTGCAAACTCACAGGGTCCCCACACAACAGTGCCCTCCAGAAG  
CAGCCCCCTCGGAGGCAGAGGAAGGAAAATGGGGATGGCTGGGGCTCTCTCCATCCTCCTTTT  
CTCCTTGCCCTTCGCATGGCTGGCCTTCCCTTCCAAACCTCCATTCCCCCTGCTGCCAGCCCC  
TTTGCCATAGCCTGATTTTGGGGAGGAGGAAGGGGCGATTTGAGGGAGAAGGGGAGAAAAGCT  
TATGGCTGGGTCTGGTTTCTTCCCTTCCCAGAGGGTCTTACTGTTCCAGGGTGGCCCCAGGG  
CAGGCAGGGGCCACACTATGCCTGTGCCCTGGTAAAGGTGACCCCTGCCATTTACCAGCAGC  
CCTGGCATGTTCTTGCCCCACAGGAATAGAATGGAGGGAGCTCCAGAACTTTCCATCCCAA  
AGGCAGTCTCCGTGGTTGAAGCAGACTGGATTTTTGCTCTGCCCTGACCCCTGTCCCTCT  
TTGAGGGAGGGGAGCTATGCTAGGACTCCAACCTCAGGGACTCGGGTGGCCTGCGCTAGCTT  
CTTTTGATACTGAAAACCTTTTAAGGTGGGAGGGTGGCAAGGGATGTGCTTAATAAATCAATT  
CCAAGCCTCAAAAAAAAAAAAAAAAAA

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FIGURE 216

MAGLAARLVLLAGAAALASGSQGDREPVYRDCVLQCEEQNCSGGALNHFRSRQPIYMSLAGW  
TCRDDCKYECMWVTVGLYLQEGHKVPQFHGKWPFSSRFLFFQEPASAVASFLNGLASLVMLCR  
YRTFVPASSPMYHTCVAFAWVSLNAFWSTVFHTRDTDLTEKMDYFCASTVILHSIYLCCVR  
TVGLQHPAVVSAFRALLLMLTVHVSYSLSLIRFDYGYNLVANVAIGLVNVVWWLAWCLWNQR  
RLPHVRKCVVVVLLQGLSLELLDFPPLFWVLDAAIWHISTIPVHVLFFSFLEDDSLYLL  
KESEDKFKLD

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## FIGURE 217

[illegible]

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FIGURE 218

MAPQSLPSSRMAPLGMLLGLLMAACFTFCLSHQNLKEFALTNPEKSSTKETERKETKAEEEL  
DAEVLEVFHPTHEWQALQPGQAVPAGSHVRLNLQTGEREAKLQYEDKFRNNLK GKRLDINTN  
TYTSQDLKSALAKFKEGAEMESSKEDKARQAEVKRLFRPIEELKKDFDELNVVIETDMQIMV  
RLINKFNSSSSSLEEKIAALFDLEYYVHQMDNAQDLLSFGGLQVVINGLNSTEPLVKEYAAF  
VLGAAFSSNPKVQVEAIEGGALQKLLVILATEQPLTAKKKVLFALCSLLRHFPYAQRQFLKL  
GGLQVLR TLVQEKGTEVLAVRVVTLLYDLVTEKMF AEEEEAE LTQEMSPEKLQYRQVHLLPG  
LWEQGWCEITAHLLALPEHDAREKVLQTLGVLLTTCRDRYRQDPQLGRTLASLQAEYQVLAS  
LELQDGEDEGYFQELLGSVNSLLKELR

TTCCGGCTTCCGTAGAGGAAGTGGCGCGGACCTTCATTTGGGGTTTCGGTTCCCCCCTTCCC  
CTTCCCCGGGGTCTCGGGGTGACATTGCACCCGCGCCCTCGTGGGGTCGCGTTGCCACCCCA  
CGCGGACTCCCCAGCTGGCGCGCCCTCCCATTTGCCTGTCTGGTCAAGCCCCCACCCCC  
TTCCCACCTGACCAGCAATGGGGCTGCGGTGTTTTTCGGCTGCACCTTCGTGCGGTTCCGGC  
CCGGCCTTCGCGCTTTTCTTGATCACTGTGGCTGGGGACCCGCTTCGCGTTATCATCCTGGT  
CGCAGGGGCATTTTTCTGGCTGGTCTCCCTGCTCCTGGCCTCTGTGGTCTGGTTTCATCTTGG  
TCCATGTGACCGACCGGTGAGATGCCCGGCTCCAGTACGGCCTCCTGATTTTTGGTGCTGCT  
GTCTCTGTCTTCTACAGGAGGTGTTCCGCTTTGCCTACTACAAGCTGCTTAAGAAGGCAGA  
TGAAGGGTTAGCATCGCTGAGTGAGGACGGAAGATCACCCATCTCCATCCGCCAGATGGCCT  
ATGTTTCTGGTCTCTCCTTCGGTATCATCAGTGGTGTCTTCTCTGTTATCAATATTTTGGCT  
GATGCACTTTGGGCCAGGTGTGGTTGGGATCCATGGAGACTCACCTATTACTTCTTGACTTC  
AGCCTTTCTGACAGCAGCCATTATCCTGCTCCATACCTTTTGGGGAGTTGTGTTCTTTGATG  
CCTGTGAGAGGAGACGGTACTGGGCTTTGGGCCTGGTGGTTGGGAGTCACCTACTGACATCG  
GGACTGACATTCTGTAACCCCTGGTATGAGGCCAGCCTGCTGCCCATCTATGCAGTCACTGT  
TTCCATGGGGCTCTGGGCCTTCATCACAGCTGGAGGGTCCCTCCGAAGTATTACAGCGCAGCC  
TCTTGTGTAAGGACTGACTACCTGGACTGATCGCCTGACAGATCCACCTGCCTGTCCACTG  
CCCATGACTGAGCCCAGCCCCAGCCCCGGTCCATTGCCACATTCTCTGTCTCCTTCTCGTC  
GGTCTACCCCACTACCTCCAGGGTTTGGCTTTGTCTTTTGTGACCGTTAGTCTCTAAGCTT  
TACCAGGAGCAGCCTGGGTTTCAGCCAGTCACTGACTGGTGGGTTTGAATCTGCACTTATCCC  
CACCACCTGGGGACCCCCCTTGTGTGCTCCAGGACTCCCCCTGTGTCACTGCTCTGCTCTCAC  
CCTGCCCAAGACTCACCTCCCTTCCCTCTGTCAGGCCGACGGCAGGAGGACAGTCGGGTGAT  
GGTGTATTCTGCCCTGCGCATCCACCCGAGGACTGAGGGAAACCTAGGGGGGACCCCTGGGC  
CTGGGGTGCCCTCCTGATGTCTCGCCCTGTATTTCTCCATCTCCAGTTCTGGACAGTGCAG  
GTTGCCAAGAAAAGGACCTAGTTTTCAGCCATTGCCCTGGAGATGAAATTAATGGAGGCTCAA  
GGATAGATGAGCTCTGAGTTTCTCAGTACTCCCTCAAGACTGGACATCTTGGTCTTTTTCTC  
AGGCCTGAGGGGAACCATTTTTGGTGTGATAAATACCCTAAACTGCCTTTTTTTCTTTTTT  
GAGGTGGGGGAGGGAGGAGGTATATTGGAACCTTCTAACCCTCCTGGGCTATATTTCTC  
TCTCGAGTTGCTCCTCATGGCTGGGCTCATTTGGTCCCTTTCTCCTTGGTCCCAGACCTT  
GGGGGAAAGGAAGGAAGTGCATGTTTGGGAACGGCATTACTGGAACATAATGGTTTTTAACCT  
CCTTAACCACCAGCATCCCTCCTCTCCCCAAGGTGAAGTGGAGGGTGTCTGTGGTGTGAGCTGGC  
CACTCCAGAGCTGCAGTGCCACTGGAGGAGTCAGACTACCATGACATCGTAGGGAAGGAGGG  
GAGATTTTTTTGTAGTTTTTAATTGGGGTGTGGGAGGGGCGGGGAGTTTTTCTATAAACTGT  
ATCATTTTCTGCTGAGGGTGGAGTGTCCCATCCTTTAATCAAGGTGATTGTGATTTTGACT  
AATAAAAAAGAATTTGTAAAAA  
AAAAA



FIGURE 220

MGAAVFFGCTFVAFGPAFALFLITVAGDPLRVIIILVAGAFFWLVSLLLASVWVFIILVHVTDR  
SDARLQYGLLIIFGAAVSVLLQEVFRFAYYKLLKKADEGLASLSEDGRSPISIRQMAYVSGLS  
FGIISGVFSVINILADALGPGVVGIIHGDSPIYFLTSAFLTAIIILLHTFWGVVFFDACERRR  
YWALGLVVGSHLLTSGLTFLNPWYEASLLPIYAVTVSMGLWAFITAGGSLRSIQRSLCKD

**FIGURE 221**

AAGCTGGTTTAAAGGAAGCAGAGGAGGGTTAGATTTCGTTGAGTGAGGACGGAAGATCAACCCA  
TTTCCATTCCGCCAGATGGCCTATGTTTCTGGTCTCTCCCTTCGGNATCATCAGTGGTGTNT  
TNTCTGTTATCAATATTTTGGCTGATGCANTTGGGCCAGGTGTGGTTGGGATCCATGGAGAC  
TCACCCTATTANTTCCTGANTTCAGCCTTTNTGACAGCAGCCATTATCCTGCTC

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FIGURE 222

GACCGACCGTTCAGATGCCCCGGTTCAGTACGGCTTCCTGATTTTTGGTGCTGCTGTNTCTG  
TCCTTCTACAGGAGGTGTTCCGCTTTGCCTANTACAAGCTGCTTAAGAAGGCAGATGAGGGG  
TTAGCATNGCTGAGTGAGGACGGAAGATCACCCATTTCCATCCGCCAGATGGCCTATGTTTN  
TGGTNTTTCCTTCGGTATCATCAGTGGTGTTTTNTCTGTTATCAATATTTTGGNTGATGCAN  
TTGGGCCAGGTGTGGTTGGGATCCATGGAGANTCACCCCTATTAATTCCTGAATTCAGCCTTT  
NTGACAGCAGCCATTATCCTGNTCCATACCTTTTGGGGAGTTGTGTTTTTTGATGCCTGTGA  
GAGGAG

FIGURE 223

NGTTGGAGAAGTGGCGCGGACNTTCATTTGGGGTTTCGGTTTCCCCCCTTTCCTTTCCCCG  
GGGTCTGGGGTGACATTGCACGGGCCCCCTCGTGGGGTCGCGTTGCCACCCACGCGGACTCC  
CCAGNTGGNGCGCCCTTCCCATTTCCTGTCTGGTCAGGCCCCACCCCCCTTCCCACNTG  
ACCAGCCATGGGGGCTGCGGTGTTTTTCGGCTGCACTTTCGTGCGGTTCGGCCCGGCCTTCG  
CGCTTTTCTTGATCACTGTGGCTGGGGACCCGCTTCGCGTTATCATCCTGGTCGCAGGGGCA  
TTTTTCTGGCTGGTCTCCCTGCTCCTGGCCTCTGTGGTCTGGTTCATCTTGGTCCATGTGAC  
CGACCGGTGAGATGCCCCGGCTCCAGTACGGCCTCCTGATTTTTGGTGCTGCTGTCTGTGCC  
TTCTACAGGAGGTGTTCCGCTTTGCCTACTACAAGCTGCTTAAGAAGGCAGATGAGGGGTTA  
GCATCGCTGAGTGAGGACGGAAGATCACCCATCTCCATCCGCCAGATGGCCTATGTTTCTGG  
TCTCTCCTTCGGTATCATCAGTGGTGTCTTCTGTGTTATCAATATTTTGGCTGATGCACTTG  
GGCCAGGTGTGGTTGGGATCCATGGAGACTCACCC

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FIGURE 224

GTAAAAGAAAAGTGGCCGGACCTTCATTGGGGTTTTCGGTTCCCCCCTTTCCCNNTTCCCCGGGG  
TCTGGGGGTGACATTGCACCGCGCCCNCTCGTGGGGTCGCGTTGCCACCCACGCGGACTCCC  
CAGNTGGCGCGCCCCCTCCCATTTGCCTGTCTTGGTCAGGCCCCACCCCCCTTCCACCTGA  
CCAGCCATGGGGGCTGCGGTGTTTTTCGGGCTGCACTTTCGTGCGGTTGCGGCCCGGCCTTC  
GCGCTTTTCTTGATCACTGTGGCTGGGGACCCGCTTCGCGTTATCATCCTGGTCGCAGGGGC  
ATTTTTCTGGCTGGTCTCCCTGCTCCTGGCCTCTGTGGTCTGGTTCATCTTGGTCCATGTGA  
CCGACCGGTCAGATGCCCCGGCTCCAGTACGGCCTCCTGATTTTTTGGTGCTGCTGTCTCTGTC  
CTTCTACAGGAGGTGTTCCGCTTTGCCTACTACAAGCTGCTTAAGAAGGCAGATGAGGGGTT  
AGCATCGCTGAGTGAGGACGGAAGATCACCCATCTCCATCCGCCAGATGGCCTATGTTTCTG  
GTCTCTCCTTCGGTATCATCAGTGGTGTCTTCTCTGTTATCAATATTTTGGCTGATGCACTT  
GGGCCAGGTGTGGTTGGGATCCATGGAGAC

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FIGURE 225

GGCCCAGGGAGCAGTGGGTGGTTATAACTCAGGCCCGGTGCCCAGAGCCCAGGAGGAGGCAG  
TGGCCAGGAAGGCACAGGCCTGAGAAGTCTGCGGCTGAGCTGGGAGCAAATCCCCACCCCC  
TACCTGGGGGACAGGGCAAGTGAGACCTGGTGAGGGTGGCTCAGCAGGCAGGGAAGGAGAGG  
TGTCTGTGCGTCCTGCACCCACATCTTTCTCTGTCCCCCTCCTTGCCCTGTCTGGAGGCTGCT  
AGACTCCTATCTTCTGAATTCTATAGTGCTGGGTCTCAGCGCAGTGCCGATGGTGGCCCCGT  
CCTTGTGGTTCCTCTCTACCTGGGGAAATAAGGTGCAGCGGCCATGGCTACAGCAAGACCCC  
CCTGGATGTGGGTGCTCTGTGCTCTGATCACAGCCTTGCTTCTGGGGGTACAGAGCATGTT  
CTCGCCAACAATGATGTTTCTGTGACCACCCCTCTAACACCGTGCCCTCTGGGAGCAACCA  
GGACCTGGGAGCTGGGGCCGGGGAAGACGCCCCGGTCGGATGACAGCAGCAGCCGCATCATCA  
ATGGATCCGACTGCGATATGCACACCCAGCCGTGGCAGGCCGCGCTGTTGCTAAGGCCCAAC  
CAGCTCTACTGCGGGCGGTGTTGGTGCATCCACAGTGGCTGCTCACGGCCGCCCCACTGCAG  
GAAGAAAGTTTTTCAGAGTCCGTCTCGGCCACTACTCCCTGTCACCAGTTTATGAATCTGGGC  
AGCAGATGTTCCAGGGGTCAAATCCATCCCCACCCCTGGCTACTCCCACCCCTGGCCACTCT  
AACGACCTCATGCTCATCAAACCTGAACAGAAGAATTGTCCTCCACTAAAGATGTCAGACCCAT  
CAACGTCTCCTCTCATTGTCCCTCTGCTGGGACAAAGTGCTTGGTGTCTGGCTGGGGGACAA  
CCAAGAGCCCCCAAGTGCACTTCCCTAAGGTCCTCCAGTGCTTGAATATCAGCGTGCTAAGT  
CAGAAAAGGTGCGAGGATGCTTACCCGAGACAGATAGATGACACCATGTTCTGCGCCGGTGA  
CAAAGCAGGTAGAGACTCCTGCCAGGGTGATTCTGGGGGGCCTGTGGTCTGCAATGGCTCCC  
TGCAGGGACTCGTGTCTTGGGGAGATTACCCTTGTGCCCCGCCCAACAGACCGGGTGTCTAC  
ACGAACCTCTGCAAGTTCACCAAGTGGATCCAGGAAACCATCCAGGCCAACTCCTGAGTCAT  
CCCAGGACTCAGCACACCGGCATCCCCACCTGCTGCAGGGACAGCCCTGACACTCCTTTTCAG  
ACCCTCATTCCTTCCCAGAGATGTTGAGAATGTTTCATCTCTCCAGCCCCTGACCCCATGTCT  
CCTGGACTCAGGGTCTGCTTCCCCACATTGGGCTGACCGTGTCTCTCTAGTTGAACCCCTGG  
GAACAATTTCCAAAACGTCCAGGGCGGGGGTTCGTCTCAATCTCCCTGGGGCACTTTCAT  
CCTCAAGCTCAGGGCCCATCCCTTCTCTGCAGCTCTGACCCAAATTTAGTCCCAGAAATAAA  
CTGAGAAGTGGAAAAAAAAA

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FIGURE 226

MATARPPMMWVLCALITALLGVTEHVLANNVSCDHPSNTVPSGSNQDLGAGAGEDARSDD  
SSSRIINGSDCDMHTQPWQAALLLRPNQLYCGAVLVHPQWLLTAAHCRKKVFRVRLGHYSLS  
PVYESGQQMFQGVKSI PHPGYSHPGHSNDLMLIKLNRRI RPTKDVRPINVSSHCP SAGTKCL  
VSGWGTTKSPQVHF PKVLQCLNISVLSQKRCEDAYPRQIDDTMFCAGDKAGR DSCQGD SGGP  
VVCNGSLQGLVSWGDYPCARPNRPGVYTNLCKFTKWIQETIQANS

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**FIGURE 227**

**ATGGTCAACGACCGGTGGAAGACCATGGGCGGCGCTGCCAACTTGAGGACCGGCCGCGCGA**  
**CAAGCCGACGCGGCCGAGCTGCGGGCTACGTGCTGTGCACCGTGTCTGGCCCTGGCTGTGC**  
**TGCTGGCTGTAGCTGTCAACGGTGCCGTGCTCTTCCTGAACCACGCCACGCGCCGGGCACG**  
**GCGCCCCACCTGTCTGTCACTGAGGCTGCGAGCGCCAAACAGCGCCCTGGTCACTGTGGA**  
**AAGGGCGGACAGCTCGCACCTCAGCATCCTCATTGACCCGCGCTGCCCCGACCTCACCGACA**  
**GCTTCGCACGCTGGAGAGCGCCAGGCCTCGGTGCTGCAGGCGCTGACAGAGCACCAGGCC**  
**CAGCCACGGCTGGTGGGCGACAGGAGCAGGAGCTGCTGGACACGCTGGCCGACCAGCTGCC**  
**CCGGCTGTGCGCCGAGCCTCAGAGCTGCAGACGAGTGCAATGGGCTGCGGAAGGGGCATG**  
**GCACGCTGGGCCAGGGCCTCAGCGCCCTGCAGAGTGAGCAGGGCCGCTCATCCAGCTTCTC**  
**TCTGAGAGCCAGGGCCACATGGCTCACCTGGTGAACCTCCGTGACGACATCCTGGATGCCCT**  
**GCAGAGGGACCGGGGGCTGGGCCGGCCCCGCAACAAGGCCGACCTTCAGAGAGCGCCTGCCC**  
**GGGGAACCCGGCCCCGGGGCTGTGCCACTGGCTCCCGCCCCGAGACTGTCTGGACGTCTCT**  
**CTAAGCGGACAGCAGGACGATGGCGTCTACTCTGTCTTTCCACCCACTACCCGGCCGGCTT**  
**CCAGGTGTACTGTGACATGCGCACGGACGGCGGGCTGGACGGTGTTCAGCGCCGGGAGG**  
**ACGGCTCCGTGAACCTTCTCCGGGGCTGGGACGCGTACCGAGACGGCTTTGGCAGGCTCACC**  
**GGGGAGCACTGGCTAGGGCTCAAGAGGATCCACGCCCTGACCACACAGGCTGCCTACGAGCT**  
**GCACGTGGACCTGGAGGACTTTGAGAATGGCACGGCCTATGCCCGCTACGGGAGCTTCGGCG**  
**TGGGCTTGTCTCCGTGGACCTGAGGAAGACGGGTACCCGCTCACCGTGGCTGACTATTCC**  
**GGCACTGCAGGCGACTCCCTCCTGAAGCACAGCGGCATGAGGTTCAACCACCAAGGACCGTGA**  
**CAGCGACCATTAGAGAACTGTGCCGCTTCTACCGCGGTGCCTGGTGGTACCGCAACT**  
**GCCACACGTCCAACCTCAATGGGCAGTACCTGCGCGGTGCGCACGCCTCCTATGCCGACGGC**  
**GTGGAGTGGTCTCCTGGACCGCTGGCAGTACTCACTCAAGTTCTCTGAGATGAAGATCCG**  
**GCGGCTCCGGGAGGACCGCTAGACTGGTGCACCTTGTCTTGGCCCTGCTGGTCCCTGTGCG**  
**CCCATCCCCGACCCACCTCACTCTTTCGTGAATGTTCTCCACCCACCTGTGCCTGGCGGAC**  
**CCACTCTCCAGTAGGGAGGGGCCGGGCCATCCCTGACACGAAGCTCCCTGGGCCGGTGAAGT**  
**CACACATCGCCTTCTCGCCGTCCCCACCCCTCCATTGGCAGCTCACTGATCTCTTGCCCT**  
**TGCTGATGGGGCTGGCAAACCTTGACGACCCCAACTCCTGCCTGCCCCACTGTGACTCCGG**  
**TGCTGTTTGCCGTCCCCCTGGCCAGGATGGTGGAGTCTGCCCCAGGCACCCCTCTGCCCTGCC**  
**GGCCAAATACCCGCATTATGGGACAGAGAGCAGGGGGCAGACAGCACCCTGGAGTCTCTC**  
**CTAGCAGATCGTGGGGAATGTACAGGTCTCTCTGAGGTACAGGTCTGAGGCCAGTATCCTCCAG**  
**CCCTCCCAATGCCAACCCCAACCCGTTTCCCTGGTGCCAGAGAACCCACCTCTCCCCCAA**  
**GGGCCTCAGCCTGGCTGTGGGTGGGTGGCCCCATCCTACCAGGCCCTGAGGTGAGGATGGG**  
**GAGCTGCTGCCTTTGGGGACCCACGCTCCAAGGCTGAGACCAGTTCCCTGGAGGCCACCCAC**  
**CCTGTGCCCCGGCAGGCCTGGGGTCTGCAGTCTCTTACCTGCTGTGCCACCTGCTCTCTG**  
**TCTCAAATGAGGCCCAACCCATCCCCACCCAGCTCCCGGCCGTCTCTACCTGGGGCAGC**  
**CGGGGCTGCCATCCCATTCTCCTGCCTCTGGAAGGTGGGTGGGCCCTGCACCGTGGGGCT**  
**GGACTGCGCTAATGGGAAGCTCTTGGTTTTCTGGGCTGGGGCTAGGCAGGGCTGGGATGAG**  
**GCTTGTACAACCCCAACCAATTTCCAGGGACTCCAGGGTCTGAGGCCTCCAGGAGG**  
**GCCTTGGGGGTGATGACCCCTTCCCTGAGGTGGCTGTCTCCATGAGGAGGCCAACCCCTGGC**  
**ATTGACCGTGGCCACCTGGACCCAGGCCAGGCCGGCCGGCCGAGTGGTCAAGGGACAGGGA**  
**CCACCTCACCGGGCAAATGGGGTGGGGGGACTGGGGCACCAGACCAGGCACCACTGGACA**  
**CTTTCTTGTGAATCCTCCCAACACCCAGCACGCTGTATCCCCACTCCTTGTGTGCACACA**  
**TGCAGAGGTGAGACCCGAGGCTCCCAGGACCAGCAGCCACAAGGGCAGGGCTGGAGCCGGG**  
**TCCTCAGCTGTCTGCTCAGCAGCCCTGGACCCGCGTGCCTTACGTACGGCCAGATGCAGGG**  
**CGGCTTTTCCAAGGCCTCCTGATGGGGCCCTCCGAAAGGCTGGAGTCAGCCTTGGGGAGCT**  
**GCCTAGCAGCCTCTCCTCGGGCAGGAGGGGAGGTGGCTTCTCCAAAGGACACCCGATGGCA**  
**GGTGCCTAGGGGGTGTGGGGTCCGTTCTCCCTTCCCTCCCACTGAAGTTTGTGCTTAAAA**  
**AACAATAAATTTGACTTGGCACCCTGGGGGTTGGTGGGAGAGGCCGTGTGACCTGGCTCTC**  
**TGTCCAGTGCCACCAGGTATCCACATGCGCAG**



FIGURE 228

MVNDRWKTMGGAAQLEDPRDKPQRPSCGYVLCTVLLALAVLLAVAVTGAVLFLNHAHAPGT  
APPPVVSTGAASANSALVTVERADSSHLSILIDPRCPDLTDSFARLESAQASVLQALTEHQA  
QPRLVGDQEQELLDTLADQLPRLRLARASELQTECMGLRKGHGTLGQGLSALQSEQGRLIQLL  
SESQGHMAHLVNSVSDILDALQDRGLGRPRNKADLQRAPARGTRPRGCATGSRPRDCLDVL  
LSGQQDDGVYSVFPPTHYPAGFQVYCDMRDGGGWTVFQRREDGSVNFFRGWDAYRDGFGRLT  
GEHWLGLKRIHALTTQAAYELHVDLEDFENGTAAYARYGSFGVGLFSVDPEEDGYPLTVADYS  
GTAGDSLLKHSGMRFTTKDRSDHSENNCAAFYRGAWWYRNCHTSNLNGQYLRGAHASADG  
VEWSSWTGWQYSLKFSEMKIRPVREDR

FIGURE 229

GCAGTCAGAGACTTCCCCTGCCCCTCGCTGGGAAAGAACATTAGGAATGCCTTTTAGTGCCT  
TGCTTCCTGAACTAGCTCACAGTAGCCCGGCGGCCAGGGCAATCCGACCACATTTCACTCT  
CACCGCTGTAGGAATCCAGATGCGAGGCCAAGTACAGCAGCACGAGGGACATGCTGGATGATG  
ATGGGGACACCACCATGAGCCTGCATTCTCAAGCCTCTGCCACAACCTCGGCATCCAGAGCCC  
CGGCGCACAGAGCACAGGGCTCCCTCTTCAACGTGGCGACCAGTGGCCCTGACCCTGCTGAC  
TTTGTGCTTGGTGCTGCTGATAGGGCTGGCAGCCCTGGGGCTTTTGTTTTTTCAGTACTACC  
AGCTCTCCAATACTGGTCAAGACACCATTTCTCAAATGGAAGAAAGATTAGGAAATACGTCC  
CAAGAGTTGCAATCTCTTCAAGTCCAGAATATAAAGCTTGCAGGAAGTCTGCAGCATGTGGC  
TGAAAACTCTGTGCTGAGCTGTATAACAAAGCTGGAGCACACAGGTGCAGCCCTTGTACAG  
AACAATGGAATGGCATGGAGACAATTGCTACCAGTTCTATAAAGACAGCAAAAGTTGGGAG  
GACTGTAAATATTTCTGCCTTAGTGAAAACTCTACCATGCTGAAGATAAAACAAACAAGAAGA  
CCTGGAATTTGCCGCTCTCAGAGCTACTCTGAGTTTTTCTACTCTTATTGGACAGGGCTTT  
TGCGCCCTGACAGTGGCAAGGCCTGGCTGTGGATGGATGGAACCCCTTTCACTTCTGAACTG  
TTCCATATTATAATAGATGTCACCAGCCCAAGAAGCAGAGACTGTGTGGCCATCCTCAATGG  
GATGATCTTCTCAAAGGACTGCAAAGAATTGAAGCGTTGTGTCTGTGAGAGAAGGGCAGGAA  
TGGTGAAGCCAGAGAGCCTCCATGTCCCCCTGAAACATTAGGCGAAGGTGACTGATTGCCC  
CTCTGCAACTACAAATAGCAGAGTGAGCCAGGCGGTGCCAAAGCAAGGGCTAGTTGAGACAT  
TGGGAAATGGAACATAATCAGGAAAGACTATCTCTCTGACTAGTACAAAATGGGTTCTCGTG  
TTTCCTGTTTCAAGGATCACCAGCATTTCTGAGCTTGGGTTTATGCACGTATTTAACAGTCACA  
AGAAGTCTTATTTACATGCCACCAACCAACCTCAGAAACCATAATGTCATCTGCCTTCTTG  
GCTTAGAGATAACTTTTAGCTCTCTTCTCTCAATGTCTAATATCACCTCCCTGTTTTTCAT  
GTCTTCCTTACACTTGGTGGAAATAAGAACTTTTTGAAGTAGAGGAAATACATTGAGGTAAC  
ATCCTTTTCTCTGACAGTCAAGTAGTCCATCAGAAATTGGCAGTCACTTCCCAGATTGTACC  
AGCAAATACACAAGGAATCTTTTTGTTTGTTCAGTTCATACTAGTCCCTTCCCAATCCAT  
CAGTAAAGACCCCATCTGCCTTGTCCATGCCGTTTCCCAACAGGGATGTCACTTGATATGAG  
AATCTCAAATCTCAATGCCTTATAAGCATTCTTCTGTGTCCATTAAGACTCTGATAATTG  
TCTCCCCTCCATAGGAATTTCTCCCAGGAAAGAAATATATCCCCATCTCCGTTTCATATCAG  
AACTACCGTCCCCGATATTCCCTTCAGAGAGATTAAAGACCAGAAAAAAGTGAGCCTCTTCA  
TCTGCACCTGTAATAGTTTCAGTTCCTATTTTCTTCCATTGACCCATATTTATACCTTTTCAG  
GTACTGAAGATTTAATAATAATAAATGTAAATACTGTGAAAAA

FIGURE 230

MQAKYSSTRDMLDDDGDTTMSLHSQASATTRHPEPRRTEHRAPSSTWRPVALTLLTLCLVLL  
IGLAALGLLFFQYYQLSNTGQDTISQMEERLGNTSQELQSLQVQNIKLAGSLQHVAEKLCRE  
LYNKAGAHRCSPCTEQWKWHGDNCYQFYKDSKSWEDCKYFCLSENSTMLKINKQEDLEFAAS  
QSYSEFFYSYWTGLLRPD SGKAWLWMDGTPFTSELFHIIIDVTSPRSRDCVAILNGMIFSKD  
CKELKRCVCERRAGMVKPESLHVPPETLGEGD

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FIGURE 231

AATTTTCACCGCTGTAGGAATCCAGATGCAGGCCAAGTACAGCAGCACGAGGGACATGNTGG  
ATGATGATGGGACACCACCATGAGCCTGCATTNTCAAGCTTTTGCCACAATTCCGGCATCCAG  
AGCCCCGGCGCACAGAGCACAGGGNTCCTTTTTCAACGTGGCGACCAGTGGCCCTGACCCTG  
CTGACTTTGTGCTTGGTGCTGCTGATAGGGCTGGCAGCCCTGGGGCTTTTGTTTTTTCAGTA  
CTACCAGCTCTCCAATACTGGTCAAGACACCATTTCTCAAATGGAAGAAAGATTAGGAAATA  
CGTCCCAAGAGTTGCAATTTNTTCAAGTCCAGAATATAAAGCTTGCAGGAAGTNTGCAGCAT  
GTGGCTGAAAACTCTGTCGTGAGCTGTATAACAAAGCTGGAGGAACCTTTGAAGGAGGGCAA  
AGTNTCCTCATNTACTATACACACACCACTTCCC

FIGURE 232

GCCGAGCGCAAGAACCCTGCGCAGCCAGAGCAGCTGCTGGAGGGGAATCGAGGCGCGGCTC  
 CGGGGATTCTGGCTCGGGCCGCTGGCTCTGCTCTGCGGGGAGGGAGCGGGCCCCCGCGGGG  
 CCCGAGCCCTCCGGATCCGCCCCCTCCCGGTCGCGCCCCCTCGGAGACTCCTCTGGCTGCT  
 CTGGGGGTTCGCGCGGGGCGGGGACCCGCGGTCCGGGCGCCATGCGGGCATCGCTGCTGCTG  
 TCGGTGCTGCGGCCCGCAGGGCCCCGTGGCCGTGGGCATCTCCCTGGGCTTCACCCCTGAGCCT  
 GCTCAGCGTCACCTGGGTGGAGGAGCCGTGCGGCCAGGCCCGCCCCAACCTGGAGACTCTG  
 AGCTGCCGCCGCGCGGCAACACCAACGCGGCGCGCCGGCCCAACTCGGTGCAGCCCGGAGCG  
 GAGCGCGAGAAGCCCGGGGCCGGCGAAGGCGCCGGGAGAATTGGGAGCCGCGCGTCTTGCC  
 CTACCACCCCTGCACAGCCCGGCCAGGCCGCCAAAAAGGCCGTGAGGACCCGCTACATCAGCA  
 CGGAGCTGGGCATCAGGCAGAGGCTGCTGGTGGCGGTGCTGACCTCTCAGACCACGCTGCCC  
 ACGCTGGGCGTGGCCGTGAACCGCACGCTGGGGCACCGGCTGGAGCGTGTGGTGTTCCTGAC  
 GGGCGCACGGGGCCGCGGGCCCCACCTGGCATGGCAGTGGTGACGCTGGGCGAGGAGCGAC  
 CCATTGGACACCTGCACCTGGCGCTGCGCCACCTGCTGGAGCAGCACGGCGACGACTTTGAC  
 TGGTTCTTCTGGTGCCTGACACCACCTACACCGAGGCGCACGGCCTGGCACGCCTAACTGG  
 CCACCTCAGCCTGGCCTCCGCGGCCACCTGTACCTGGGCCGGCCCCAGGACTTCATCGGCG  
 GAGAGCCCCACCCCGGCCGCTACTGCCACGGAGGCTTTGGGGTGCTGCTGTGCGCATGCTG  
 CTGCAACAACCTGCGCCCCACCTGGAAGGCTGCCGCAACGACATCGTCAGTGCGCGCCCTGA  
 CGAGTGGCTGGGTGCTGCAATCTCGATGCCACCGGGGTGGGCTGCACTGGTGACCACGAGG  
 GGGTGCACTATAGCCATCTGGAGCTGAGCCCTGGGGAGCCAGTGACAGAGGGGGACCCCTCAT  
 TTCCGAAGTGCCCTGACAGCCACCCCTGTGCGTGACCCTGTGCACATGTACCAGCTGCACAA  
 AGCTTTCGCCCAGCTGAACTGGAACGCACGTACCAGGAGATCCAGGAGTTACAGTGGGAGA  
 TCCAGAATACCAGCCATCTGGCCGTTGATGGGGACCGGGCAGCTGCTTGGCCCCGTGGTATT  
 CCAGCACCATCCCGCCCCGCGCTCCCGCTTTGAGGTGCTGCGCTGGGACTACTTCACGGAGCA  
 GCACGCTTCTCCTGCGCCGATGGCTCACCCCGCTGCCACTGCGTGGGGCTGACCGGGCTG  
 ATGTGGCCGATGTTCTGGGGACAGCTCTAGAGGAGCTGAACCGCCGCTACCACCCGGCCTTG  
 CGGCTCCAGAAGCAGCAGCTGGTGAATGGCTACCGACGCTTTGATCCGGCCCCGGGTATGGA  
 ATACACGCTGGACTTGACAGCTGGAGGCACTGACCCCCAGGGAGGCCGCGCGCCCCCTACTC  
 GCCGAGTGCACTGCTCCGGCCGCTGAGCCGCGTGGAGATCTTGCTGTGCCCTATGTCACT  
 GAGGCCTCACGTCTCACTGTGCTGCTGCCCTCTAGCTGCGGCTGAGCGTGACCTGGCCCCCTGG  
 CTTCTTGAGGCTTTTGCCACTGCAGCACTGGAGCCTGGTGATGCTGCGGCAGCCCTGACCC  
 TGCTGCTACTGTATGAGCCGCGCCAGGCCAGCGCGTGGCCCATGCAGATGTCTTCGCACCT  
 GTCAAGGCCCCAGTGGCAGAGCTGGAGCGGCGTTTCCCCGGTGCCCCGGGTGCCATGGCTCAG  
 TGTGCAGACAGCCGCACCCCTACCACTGCGCCTCATGGATCTACTCTCCAAGAAGCACCCGC  
 TGGACACACTGTTCTGCTGGCCGGGCCAGACACGGTGCTCACGCCTGACTTCTGAACCGC  
 TGCCGCTATGCATGCCATCTCCGGCTGGCAGGCCTTCTTTCCCATGCATTTCCAAGCCTTCCA  
 CCCAGGTGTGGCCCCACCACAAGGCGCTGGGCCCCCCAGAGCTGGGCCGTGACACTGGCCGCT  
 TTGATCGCCAGGCAGCCAGCGAGGCTGCTTCTACAACCTCCGACTACGTGGCAGCCCGTGGG  
 CGCCTGGCGGCAGCCTCAGAACAAGAAGAGGAGCTGCTGGAGAGCCTGGATGTGTACGAGCT  
 GTTCTCTCACTTCTCCAGTCTGCATGTGCTGCGGGCGGTGGAGCCGGCGCTGCTGCAGCGCT  
 ACCGGGCCCCAGAGCTGCAGCGCGAGGCTCAGTGAGGACCTGTACCACCGCTGCCCTCAGAGC  
 GTGCTTGAGGGCCTCGGCTCCCGAACCCAGCTGGCCATGCTACTCTTTGAACAGGAGCAGGG  
 CAACAGCACCTGACCCCCACCCCTGTCCCCGTGGGCCGTGGCATGGCCACACCCACCCCACTT  
 CTCCCCCAAACAGAGCCACCTGCCAGCCTCGCTGGGCAGGGCTGGCCGTAGCCAGACCCC  
 AAGCTGGCCCACTGGTCCCCTCTCTGGCTCTGTGGTCCCTGGGCTCTGGACAAGCACTGGG  
 GGACGTGCCCCCAGAGCCACCCACTTCTCATCCCAAACCCAGTTTCCCTGCCCCCTGACGCT  
 GCTGATTGCGGCTGTGGCCTCCACGTATTTATGCAGTACAGTCTGCCTGACGCCAGCCCTGC  
 CTCTGGGCCCTGGGGCTGGGCTGTAGAAGAGTTGTGGGGAAGGAGGAGCTGAGGAGGGG  
 GCATCTCCAACTTCTCCCTTTTGGACCCTGCCGAAGCTCCCTGCCTTTAATAAACTGGCCA  
 AGTGTGGA AAAA

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FIGURE 233

MRASLLLSVLRPAGPVAVGISLGFTLSLLSVTWVEEPCGPGPPQPGDSELPPRGNTNAARRP  
NSVQPGAEREKPGAGEGAGENWEPRVLPYHPAQPGQAAKKAVRTRYISTELGIRQLLVAVL  
TSQTTLPTLGVAVNRTLGHRLERVVFLTGARGRRAPPGMAVVTLGEEPIGHLHLALRHLL  
QHGDDEFDWFLLVPDTTYTEAHGLARLTGHLSLASAAHLYLGRPQDFIGGEPTPGRYCHGGFG  
VLLSRMLLQQLRPHLEGCRNDIVSARPDEWLGRCILDATGVGCTGDHEGVHYSHLELSPGEP  
VQEGDPHFRSALTAPVRDPVHMYQLHKAFARAELETTYQEIQELQWEIQNTSHLAVDGDRA  
AAWPVGIPAPSRPASRFEVLRWDYFTEQHAFSCADGSPRCPLRGADRADVADVLTAL EELN  
RRYHPALRLQKQQLVNGYRRFDPARGMEYTLDLQLEALTPQGGRRPLTRRVQLLRPLSRVEI  
LPVPYVTEASRLTVLLPLAAAERDLAPGFLEAFATAALEPGDAAAALTLLLLYEPRQAQRVA  
HADVFAPVKAHVAELERRFPGARVPWLSVQTAAPSPLRLMDLLSKKHPLDTLFLLAGPDTV  
TPDFLNRCRMHAISGWQAFFPMHFQAFHPGVAPPQPGPPPELGRDTGRFDRQAASEACFYNS  
DYVAARGRLAAASEQEEELLES LDVYELFLHFSSHLVLR AVEPALLQRYRAQTCSARLSEDL  
YHRCLQSVLEGLGSRTQLAMLLFEQE QGNST

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FIGURE 234

GCTCTGGCCGGCCCCGGCGATTGGTCACCGCCCGCTAGGGGACAGCCCTGGCCTCCTCTGAT  
TGGCAAGCGCTGGCCACCTCCCCACACCCCTTGCGAACGCTCCCCTAGTGGAGAAAAGGAGT  
AGCTATTAGCCAATTTCGGCAGGGCCCCGCTTTTTAGAAAGCTTGATTTCTTTGAAGATGAAAG  
ACTAGCGGAAGCTCTGCCTCTTTCCCCAGTGCGGCGAGGGAACTCGGGGCGATTGGCTGGGAA  
CTGTATCCACCCAAATGTCACCGATTTCTTCTATGCAGGAAATGAGCAGACCCATCAATAA  
GAAATTTCTCAGCCTGGCCGAAAAATGGTTGGCCCCACGAAGCCACGACAACCTGGAGGCAAAG  
AGGGTTGCTCAACGCCCCGCTCATTGGAAAACCAAATCAGATCTGGGACCTATATAGCGTG  
GCGGAGGCGGGCGATGATTGTCGCGCTCGCACCCACTGCAGCTGCGCACAGTCGCATTTCT  
TTCCCCGCCCCCTGAGACCCTGCAGCACCATCTGTCATGGCGGCTGGGCTGTTTGGTTTGAGC  
GCTCGCCGTCTTTTGGCGGCAGCGGCGACGCGAGGGCTCCCGGCCGCCCGCTCCGCTGGGA  
ATCTAGCTTCTCCAGGACTGTGGTCGCCCCGTCCGCTGTGGCGGGAAAGCGGCCCCCAGAAC  
CGACCACACCGTGGCAAGAGGACCCAGAACCCGAGGACGAAAACCTTGTATGAGAAGAACCCA  
GACTCCCATGGTTATGACAAGGACCCCGTTTTGGACGTCTGGAACATGCGACTTGTCTTCTT  
CTTTGGCGTCTCCATCATCCTGGTCCTTGGCAGCACCTTTGTGGCCTATCTGCCTGACTACA  
GGATGAAAGAGTGGTCCCGCCGCGAAGCTGAGAGGCTTGTGAAATACCGAGAGGCCAATGGC  
CTTCCCATCATGGAATCCAACCTGCTTCGACCCCAGCAAGATCCAGCTGCCAGAGGATGAGTG  
ACCAGTTGCTAAGTGGGGCTCAAGAAGCACCGCCTTCCCCACCCCTGCCTGCCATTCTGAC  
CTCTTCTCAGAGCACCTAATTAAAGGGGCTGAAAGTCTGAA

**FIGURE 235**

MAAGLFGLSARRLLAAAATRGLPAARVRWESSFSRTVVAPSAVAGKRPPEPTTPWQEDPEPE  
DENLYEKNPDSHGYDKDPVLDVWNMRLVFFFGVSIILVLGSTFVAYLPDYRMKEWSRREAER  
LVKYREANGLPIMESNCFDPSKIQLPEDE



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FIGURE 236

GGCGGCTGGGCTGTTTGGTTTGAGCGCTCGCCGTCTTTTGGCGGCAGCGGCGACGCGAGGGC  
TCCCGGCCGCCCCGCTCCGCTGGGAATCTAGCTTCTCCAGGACTGTGGTCGCCCCGTCCGCT  
GTGGCGGGAAAGCGGCCCCCAGAACCGACCACACCGTGGCAAGAGGACCCAGAACCCGAGGA  
CGAAAACCTTGTATGAGAAGAACCAGACTCCCATGGTTATGACAAGGACCCCGTTTTGGACG  
TCTGGAACATGCGACTTGTCTTCTTCTTTGGCGTCTCCATCATCCTGGTCCTTGGCAGCACC  
TTTGTGGCCTATCTGCCTGACTACAGGATGAAAGAGTGGTCCCGCCGCGAAGCTGAGAGGCT  
TGTGAAATACCGAGAGGCCAATGGCCTTCCCATCATGGAATCCAACCTGCTTCGACCCAGCA  
AGATCCAG

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FIGURE 237

GCGGCGGCTATGCGCTTGCTCTGCTCGTCCTGTTGCTCCTGGGGCCCGGCGGCTGGTGCCT  
TGCAGAACCCCAACGCGACAGCCTGCGGGAGGAACTTGTATCACCCCGCTGCCTTCCGGGG  
ACGTAGCCGCCACATTCCAGTTCCGCACGCGCTGGGATTTCGGAGCTTCAGCGGGAAGGAGTG  
TCCCATTACAGGCTCTTTCCCAAAGCCCTGGGGCAGCTGATCTCCAAGTATTCTCTACGGGA  
GCTGCACCTGTCAATTCACACAAGGCTTTTGGAGGACCCGATACTGGGGGCCACCCTTCCTGC  
AGGCCCCATCAGGTGCAGAGCTGTGGGTCTGGTTCCAAGACACTGTCACTGATGTGGATAAA  
TCTTGGAAGGAGCTCAGTAATGTCCTCTCAGGGATCTTCTGCGCCTCTCTCAACTTCATCGA  
CTCCACCAACACAGTCACTCCCACTGCCTCCTTCAAACCCCTGGGTCTGGCCAATGACACTG  
ACCACTACTTTCTGCGCTATGCTGTGCTGCCGCGGGAGGTGGTCTGCACCGAAAACCTCACC  
CCCTGGAAGAAGCTCTTGCCCTGTAGTTCCAAGGCAGGCCTCTCTGTGCTGCTGAAGGCAGA  
TCGCTTGTTCCACACCAGCTACCACTCCCAAGGCAGTGCATATCCGCCCTGTTTGCAGAAATG  
CACGCTGTACTAGCATCTCCTGGGAGCTGAGGCAGACCCTGTCAGTTGTATTTGATGCCTTC  
ATCACGGGGCAGGGAAAGAAAGACTGGTCCCTCTTCCGGATGTTCTCCCGAACCCCTCACGGA  
GCCCCTGCCCCCTGGCTTCAGAGAGCCGAGTCTATGTGGACATCACCACTACAACCAGGACA  
ACGAGACATTAGAGGTGCACCCACCCCGACCACTACATATCAGGACGTCACTCTAGGCACT  
CGGAAGACCTATGCCATCTATGACTTGCTTGACACCGCCATGATCAACAACCTCTCGAAACCT  
CAACATCCAGCTCAAGTGGAAGAGACCCCAAGAGATGAGGCCCCCAGTGCCCTTCCTGC  
ATGCCCAGCGGTACGTGAGTGGCTATGGGCTGCAGAAGGGGAGCTGAGCACACTGCTGTAC  
AACACCCACCCATACCGGGCTTCCCGGTGCTGCTGCTGGACACCGTACCCTGGTATCTGCG  
GCTGTATGTGCACACCCTCACCATCACCTCCAAGGGCAAGGAGAACAAACCAAGTTACATCC  
ACTACCAGCCTGCCCAGGACCGGCTGCAACCCACCTCCTGGAGATGCTGATTCAGCTGCCG  
GCCAACTCAGTCACCAAGGTTTCCATCCAGTTTGAGCGGGCGCTGCTGAAGTGGACCGAGTA  
CACGCCAGATCCTAACCATGGCTTCTATGTCAGCCCATCTGTCTCAGCGCCCTTGTGCCCA  
GCATGGTAGCAGCCAAGCCAGTGGACTGGGAAGAGAGTCCCTCTTCAACAGCCTGTTCCCA  
GTCTCTGATGGCTCTAACTACTTTGTGCGGCTCTACACGGAGCCGCTGCTGGTGAACCTGCC  
GACACCGGACTTCAGCATGCCCTACAACGTGATCTGCCTCACGTGCACTGTGGTGGCCGTGT  
GCTACGGCTCCTTCTACAATCTCCTCACCCGAACCTTCCACATCGAGGAGCCCCGCACAGGT  
GGCCTGGCCAAGCGGCTGGCCAACCTTATCCGGCGCGCCGAGGTGTCCCCCACTCTGATT  
CTTGCCCTTTCCAGCAGCTGCAGCTGCCGTTTCTCTCTGGGGAGGGGAGCCCAAGGGCTGTT  
TCTGCCACTTGCTCTCCTCAGAGTTGGCTTTTGAACCAAAGTGCCCTGGACCAGGTGAGGGC  
CTACAGCTGTGTTGTCCAGTACAGGAGCCACGAGCCAAATGTGGCATTGTAATTTGAATTAA  
CTTAGAAATTCAATTCCTCACCTGTAGTGGCCACCTCTATATTGAGGTGCTCAATAAGCAAA  
AGTGGTCCGTGGCTGCTGTATTGGACAGCACAGAAAAAGATTTCCATCACCAAGAAAGGTC  
GGCTGGCAGCACTGGCCAAGGTGATGGGGTGTGCTACACAGTGTATGTCACTGTGTAGTGA  
TGGAGTTTACTGTTTGTGGAATAAAAAACGGCTGTTTCCGTGGAATAAAAAAAAAA

FIGURE 238

MPLALLVLLLLGPGGWCLAEPFRDSLREELVITPLPSGDVAATFCFRTRWDSELQREGVSHY  
RLFPKALGQLISKYSLRELHLSFTQGFWRTYWGPPFLQAPSGAELWVWFQDTVTDVDSWK  
ELSNVLSGIFCASLNFIDSTNTVTPTASFKPLGLANDTDHYFLRYAVLPREVVCTENLTPWK  
KLLPCSSKAGLSVLLKADRLFHTSYHSQAVHIRPVCNARCTSSISWELRQTLSVVFDAFITG  
QGKKDWSLFRMFSRTLTEPCPLASESRVYVDITTYNQDNETLEVHPPPTTTYQDVILGTRKT  
YAIYDLLDTAMINNSRNLNIQLKWKRPPENEAPPVPFLHAQRYVSGYGLQKGELSTLLYNTH  
PYRAFPVLLLDTPWYLRLYVHTLTITSKGKENKPSYIHYQPAQDRLQPHLLEMLIQLPANS  
VTKVSIQFERALLKWTEYTPDPNHGFYVSPSVLSALVPSMVAAPVDWEESPLFNSLFPVSD  
GSNYFVRLYTEPLLVLNLPDPFSMPYNVICLTCTVVAVCYGSFYNNLLTRTFHIEEPRTGGLA  
KRLANLIRRARGVPPL

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FIGURE 239

CAACAATGGGGTCCAGCAGCTTCTTGGTCCTCATGGTGTCTCTCGTTCTTGTGACCCTGGTGG  
CTGTGGAAGGAGTTAAAGAGGGTATAGAGAAAGCAGGGGTTTGCCCAGCTGACAACGTACGC  
TGCTTCAAGTCCGATCCTCCCCAGTGTACACAGACCAGGACTGTCTGGGGGAAAGGAAGTG  
TTGTTACCTGCACTGTGGCTTCAAGTGTGTGATTCTGTGAAGGAACTGGAAGAAGGAGGAA  
ACAAGGATGAAGATGTGTCAAGGCCATACCCTGAGCCAGGATGGGAGGCCAAGTGTCCAGGC  
TCCTCCTCTACCAGGTGTCTCAGAAATGATGCTGGGTCTTTCTACCTCTGGGGGTCACTC  
TCACTTGGCACCTGCCCCCTGAGGGTCCTGAGACTTGGAATATGGAAGAAGCAATACCCAACC  
CCACCAAAGAAAACCTGAGCTTGAAGTCCTTTTCCCCAAAAGAGGGAAGAGTCACAAAAAG  
TCCAGACCCCAGGGACGGTACTTTCCCTCTCTACCTGGTGCTCCTCCCTAATGCTCATGAAT  
GGACCCCTCATGAATGAAACCAGTGCCCTTATAAGAGACCCCAAAGAGCTGCCTTGCCCTTC  
TGCAATGTGTGATCACAGCTAGAAGGCACTGTCAGAGAAGAGAAAAGTGGTCCTCACCAGATG  
CTGAATCTGCTGGTGCCTTGATCTTGGACTTCCCAGCCTCTAGAACTGTAAGAAATAAATAT  
TTGCTGTTTATAATCCAA

FIGURE 240

MGSSSFVLVLMVSLVLVTLVAVEGVKEGIEKAGVCPADNVRCFKSDPPQCHTDQDCLGERKCC  
YLHCGFKCVIPVKELEEGGNKDEDVSRPYPEPGWEAKCPGSSSTRCPQK

FIGURE 241

AAACTCAGCACTTGCCGGAGTGGCTCATTGTTAAGACAAAGGGTGTGCACTTCCTGGCCAGG  
AAACCTGAGCGGTGAGACTCCCAGCTGCCTACATCAAGGCCCCAGGACATGCAGAACCTTCC  
TCTAGAACCCGACCCACCACCATGAGGTCTGCCTGTGGAGATGCAGGCACCTGAGCCAAGG  
CGTCCAGTGGTCTTGCTTCTGGCTGTCTGGTCTTCTTTCTCTTCGCCTTGCCCTCTTTTA  
TTAAGGAGCCTCAAACAAAGCCTTCCAGGCATCAACGCACAGAGAACATTAAAGAAAGGTCT  
CTACAGTCCCTGGCAAAGCCTAAGTCCCAGGCACCCACAAGGGCGAGGAGGACAACCATCTA  
TGCAGAGCCAGCGCCAGAGAACAATGCCCTCAACACACAAACCCAGCCCAAGGCCCCACCA  
CCGGAGACAGAGGAAAGGAGGCCAACCAGGCACCGCCGGAGGAGCAGGACAAGGTGCCCCAC  
ACAGCACAGAGGGCAGCATGGAAGAGCCAGAAAAAGAGAAAACCATGGTGAACACACTGTC  
ACCCAGAGGGCAAGATGCAGGGATGGCCTCTGGCAGGACAGAGGCACAATCATGGAAGAGCC  
AGGACACAAAGACGACCCAAAGGAAATGGGGGCCAGACCAGGAAGCTGACGGCCTCCAGGACG  
GTGTGAGAGAAGCACCCAGGGCAAAGCGGCAACCACAGCCAAGACGCTCATTCCCAAAAGTCA  
GCACAGAATGCTGGCTCCACAGGAGCAGTGTCAACAAGGACGAGACAGAAAGGAGTGACCA  
CAGCAGTCATCCACCTAAGGAGAAGAAACCTCAGGCCACCCACCCCTGCCCTTTCCAG  
AGCCCCACGACGCAGAGAAACCAAAGACTGAAGGCCGCCAACTTCAAATCTGAGCCTCGGTG  
GGATTTTGAGGAAAAATACAGCTTCGAAATAGGAGGCCTTCAGACGACTTGCCCTGACTCTG  
TGAAGATCAAAGCCTCCAAGTCGCTGTGGCTCCAGAAACTCTTTCTGCCCAACCTCACTCTC  
TTCCTGGACTCCAGACACTTCAACCAGAGTGAGTGGGACCGCCTGGAACACTTTGCACCACC  
CTTTGGCTTCATGGAGCTCAACTACTCCTTGGTGAGAAGGTCTGTACACGCTTCCCTCCAG  
TGCCCCAGCAGCAGCTGCTCCTGGCCAGCCTCCCCGCTGGGAGCCTCCGGTGCATCACCTGT  
GCCGTGGTGGGCAACGGGGGCATCCTGAACAACTCCACATGGGCCAGGAGATAGACAGTCA  
CGACTACGTGTTCCGATTGAGCGGAGCTCTCATTAAAGGCTACGAACAGGATGTGGGGACTC  
GGACATCCTTCTACGGCTTTACCGCCTTCTCCCTGACCCAGTCACTCCTTATATTGGGCAAT  
CGGGGTTTCAAGAACGTGCCTCTTGGGAAGGACGTCCGCTACTTGCACTTCCTGGAAGGCAC  
CCGGGACTATGAGTGGCTGGAAGCACTGCTTATGAATCAGACGGTGATGTCAAAAAACCTTT  
TCTGGTTTCAGGCACAGACCCAGGAAGCTTTTCGGGAAGCCCTGCACATGGACAGGTACCTG  
TTGCTGCACCCAGACTTTCTCCGATACATGAAGAACAGGTTTCTGAGGTCTAAGACCCTGGA  
TGGTGCCCCACTGGAGGATATACCGCCCCACCACTGGGGCCCTCCTGCTGCTCACTGCCCTTC  
AGCTCTGTGACCAGGTGAGTGCTTATGGCTTCATCACTGAGGGCCATGAGCGCTTTTCTGAT  
CACTACTATGATACATCATGGAAGCGGCTGATCTTTTACATAAACCATGACTTCAAGCTGGA  
GAGAGAAGTCTGGAAGCGGCTACACGATGAAGGGATAATCCGGCTGTACCAGCGTCCTGGTC  
CCGGAACCTGCCAAAGCCAAGAACTGACCGGGGGCCAGGGCTGCCATGGTCTCCTTGCCCTGCTC  
CAAGGCACAGGATACAGTGGGAATCTTGAGACTCTTTGGCCATTTCCCATGGCTCAGACTAA  
GCTCCAAGCCCTTCAGGAGTTCCAAGGGAACACTTGAACCATGGACAAGACTCTCTCAAGAT  
GGCAAATGGCTAATTGAGGTTCTGAAGTTCTTCAGTACATTGCTGTAGGTCTTGAGGCCAGG  
GATTTTAAATTAAATGGGGTGATGGGTGGCCAATACCACAATTCTGCTGAAAAACACTCTT  
CCAGTCCAAAAGCTTCTTGATACAGAAAAAGAGCCTGGATTTACAGAAACATATAGATCTG  
GTTTGAATTCCAGATCGAGTTTACAGTTGTGAAATCTTGAAGGTATTACTTAACTTCACTAC  
AGATTGTCTAGAAGACCTTTCTAGGAGTTATCTGATTCTAGAAGGGTCTATACTTGTCTTG  
TCTTTAAGCTATTTGACAACTCTACGTGTTGTAGAAAACTGATAATAATACAAATGATTGTT  
GTCCATGGAAAGGCAAATAAATTTTCTACAGTGAAAAA

FIGURE 242

MRSCLWRCRHLSQGVQWSLLLAVLVFFLFALPSFIKEPQTKPSRHQRTENIKERSLQSLAKP  
KSQAPTRARRTTIYAEPAPENNALNTQTQPKAHTTGDRGKEANQAPPEEQDKVPHTAQRAAW  
KSPEKEKTMVNTLSPRGQDAGMASGRTEAQSWKSQDTKTTQGNGGQTRKLTASRTVSEKHQG  
KAATTAKTLIPKSQHRMLAPTGA VSTRTRQKGVTTAVIPPEKKKPQATPPPAPFQSPTTQRN  
QRLKAANFKSEPRWDFEEKYSFEIGGLQTTCPDSVKIKASKSLWLQKLFLPNLTLFLDSRHF  
NQSEWDRLEHFAPPFGMELNYSLVQKVTRFPVPQQQLLLASLPAGSLRCITCAVVGNGG  
ILNNSHMGQEIDSHDYVFRLSGALIKGYEQDVGTRTSFYGF TAFSLTQSLILGNRGFKNVP  
LGKDVRYLHFLEGTRDYEWLEALLMNQTVMSKNLFWFRHRPQEA FREALHMDRYLLLHPDFL  
RYMKNRFLRSKTL DGAHWRIYRPTTGALLLLTALQLCDQVSAYGFITEGHERFSDHYDTSW  
KRLIFYINHDFKLEREVWKRLHDEGIIRLYQRPGPGTAKAKN

FIGURE 243

CGATGCGCGGACCCGGGCACCCCTCCTCCTGGGGCTGCTGCTGGTGCTGGGGCCTTCGCCG  
GAGCAGCGAGTGGAATTTGTTCTCGAGATCTGAGGATGAAGGACAAGTTTCTAAACACCT  
TACAGGCCCTCTTTATTTTAGTCCAAAGTGCAGCAAACACTTCCATAGACTTTATCACAACA  
CCAGAGACTGCACCATTCCTGCATACTATAAAAGATGCGCCAGGCTTCTTACCCGGCTGGCT  
GTCAGTCCAGTGTGCATGGAGGATAAGTGAAGCAGACCGTACAGGAGCAGCACACCAGGAGCC  
ATGAGAAGTGCCTTGGAACCAACAGGGAAACAGAACTATCTTTATACACATCCCCTCATGG  
ACAAGAGATTTATTTTGCAGACAGACTCTCCATAAGTCCTTTGAGTTTTGTATGTTGTTG  
ACAGTTTGCAGATATATATTCGATAAATCAGTGTACTTGACAGTGTTATCTGTCACTTATTT



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FIGURE 244

MRGPGHPLLLGLLLVLGPSPEQRVEIVPRDLRMKDKFLKHLTGPLYFSPKCSKHFHRLYHNT  
RDCTIPAYYKRCARLLTRLAVSPVCMEDK

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FIGURE 245

GGGCTGGGCCCCGCGCAGCTCCAGCTGGCCGGCTTGGTCCTGCGGTCCCTTCTCTGGGAGG  
CCCGACCCCGCGCGCCAGCCCCACCATGCCACCCGCGGGGCTCCGCCGGGCGCGCCG  
CTCACCGCAATCGCTCTGTTGGTGCTGGGGGCTCCCCTGGTGCTGGCCGGCGAGGACTGCCT  
GTGGTACCTGGACCGGAATGGCTCCTGGCATCCGGGGTTTAACTGCGAGTTCTTCACCTTCT  
GCTGCGGGACCTGCTACCATCGGTACTGCTGCAGGGACCTGACCTTGCTTATCACCGAGAGG  
CAGCAGAAGCACTGCCTGGCCTTCAGCCCCAAGACCATAGCAGGCATCGCCTCAGCTGTGAT  
CCTCTTTGTTGCTGTGGTTGCCACCACCATCTGCTGCTTCCTCTGTTCTGTTGCTACCTGT  
ACCGCCGGCGCCAGCAGCTCCAGAGCCCATTGAAGGCCAGGAGATTCCAATGACAGGCATC  
CCAGTGACGCCAGTATACCCATACCCCCAGGACCCCCAAAGCTGGCCCTGCACCCCCACAGCC  
TGGCTTCATGTACCCACCTAGTGGTCCTGCTCCCCAATATCCACTCTACCCAGCTGGGCCCC  
CAGTCTACAACCCTGCAGCTCCTCCTCCCTATATGCCACCACAGCCCTCTTACCCGGGAGCC  
TGAGGAACCAGCCATGTCTCTGCTGCCCCCTTCAGTGATGCCAACCTTGGGAGATGCCCTCAT  
CCTGTACCTGCATCTGGTCCTGGGGGTGGCAGGAGTCCTCCAGCCACCAGGCCCCAGACCAA  
GCCAAGCCCTGGGCCCTACTGGGGACAGAGCCCCAGGGAAGTGGAACAGGAGCTGAACTAGA  
ACTATGAGGGGTTGGGGGAGGGCTTGGAATTATGGGCTATTTTTACTGGGGGCAAGGGAGG  
GAGATGACAGCCTGGGTACAGTGCCTGTTTTCAAATAGTCCCTCTGCTCCCAAGATCCCAG  
CCAGGAAGGCTGGGGCCCTACTGTTTGTCCCCTCTGGGCTGGGGTGGGGGAGGGAGGAGGT  
TCCGTCAGCAGCTGGCAGTAGCCCTCCTCTCTGGCTGCCCCACTGGCCACATCTCTGGCCTG  
CTAGATTAAAGCTGTAAAGACAAAA

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FIGURE 246

MPPAGLRRAAPLTAIALLVLGAPLVLAGEDCLWYLDNRGSHWPGFNCEFFTFCCGTCYHRYC  
CRDLTLLITERQQKHCLAFSPKTIAGIASAVILFVAVVATTICCFLCSCCYLYRRRQQLQSP  
FEGQEIPMTGIPVQPVYPYPQDPKAGPAPPQPGFMYPPSGPAPQYPLYPAGPPVYNPAAPP  
YMPPQPSYPGA

FIGURE 247

GGGGGAGCTAGGCCGGCGGCAGTGGTGGTGGCGGCGGCGCAAGGGTGAGGGCGGCCCCAGAA  
CCCCAGGTAGGTAGAGCAAGAAGATGGTGTCTTGCCCCCTCAAATGGTCCCTTGCAACCATG  
TCATTTCTACTTTCCCTCACTGTTGGCTCTCTTAAGTGTGTCCACTCCTTCATGGTGTGAGAG  
CACTGAAGCATCTCCAAAACGTAGTGATGGGACACCATTTCCCTTGGAATAAAATACGACITTC  
CTGAGTACGTCACTCCAGTTCATTATGATCTCTTGATCCATGCAAAACCTTACCACGCTGACC  
TTCTGGGGAACCAAGTAGAAATCACAGCCAGTCAGCCCACCAGCACCATCATCCTGCA  
TAGTCACCACCTGCAGATATCTAGGGCCACCCTCAGGAAGGGAGCTGGAGAGAGGCTATCGG  
AAGAACCCTGCAGGTCTGGAACACCCCCCTCAGGAGCAAAATGCACTGCTGGCTCCCGAG  
CCCCCTCCTTGTCGGGCTCCCGTACACAGTTGTCACTTCACTATGCTGGCAATCTTTCCGGAGAC  
TTTCCACGGATTTTACAAAAGCACCTACAGAACCAAGGAAGGGGAACTGAGGATACTAGCAT  
CAACACAATTTGAACCCACTGCAGCTAGAATGGCCTTTCCCTGCTTTGATGAACCTGCCTTC  
AAAGCAAGTTTCTCAATCAAAATTAGAAGAGAGCCAAGGCACCTAGCCATCTCCAATATGCC  
ATTGGTGAAATCTGTGACTGTTGCTGAAGGACTCATAGAAGACCATTTTGATGTCACGTGA  
AGATGAGCACCTATCTGGTGGCCTTCATCATTTTCAAGATTTTGAGTCTGTCAAGATAACC  
AAGAGTGGAGTCAAGGTTTCTGTTTATGCTGTGCCAGACAAGATAAATCAAGCAGATTATGC  
ACTGGATGCTGCGGTGACTCTTCTAGAATTTTATGAGGATTATTTCAAGCATACCGTATCCCC  
TACCCAAACAAGATCTTGCTGCTATTTCCCGACTTTCAGTCTGGTGTATGGAAGAACTGGGGA  
CTGACAACATATAGAGAATCTGCTCTGTTGTTTATGATGCAGAAAAGTCTTCTGCATCAAGTAA  
GCTTGGCATCACAGTGACTGTGGCCCATGAACTGGCCACCAGTGGTTTGGGAACCTGGTCA  
CTATGGAATGGTGGAAATGATCTTTGGCTAAATGAAGGATTTGCCAAATTTATGGAGTTTGTG  
TCTGTCAAGTGTGACCCATCCTGAACTGAAAGTTGGAGATTATTTCTTTGGCAAATGTTTTGA  
CGCAATGGAGGTAGATGCTTTAAATTCCTCACACCCTGTGTCTACACCTGTGGAAGAACTCCTG  
CTCAGATCCGGGAGATGTTTGATGATGTTTCTTATGATAAGGGAGCTTGTTATTCTGAATATG  
CTAAGGGAGTATCTTAGCGCTGACGCATTTAAAAGTGGTATTGTACAGTATCTCCAGAAGCA  
TAGCTATAAAAAATACAAAAACGAGGACCTGTGGGATAGTATGGCAAGTATTTGCCCTACAG  
ATGGTGTAAAAGGGATGGATGGCTTTTGCTCTAGAAGTCAACATTCATCTTCATCCTCACAT  
TGGCATCAGGAAGGGGTGGATGTGAAAACCATGATGAACACTTGGACACTGCAGAGGGGTTT  
TCCCCTAATAACCATCACAGTGAGGGGGAGGAATGTACACATGAAGCAAGCACTACATGA  
AGGGCTCTGACGGCGCCCCGGACACTGGGTACCTGTGGCATGTTCCATTGACATTCATCACC  
AGCAAATCCAACATGGTCCATCGATTTTGTCTAAAAACAAAAACAGATGTGCTCATCCTCCC  
AGAAGAGGTGGAATGGATCAAATTTAATGTGGGCATGAATGGCTATTACATTGTGCATTACG  
AGGATGATGGATGGGACTCTTTGACTGGCCTTTTAAAAGGAACACACACAGCAGTCAGCAGT  
AATGATCGGGCAAGTCTCATTAACAATGCATTTTCAAGTCTGTCAGCATTGGGAAGCTGTCCAT  
TGAAAAGGCCTTGGATTTATCCCTGTACTTGAAACATGAACTGAAATTATGCCCGTGTTC  
AAGGTTTGAATGAGCTGATTCTATGTATAAGTTAATGGAGAAAAGAGATATGAATGAAGTG  
GAAACTCAATTCAAGGCCTTCTCATCAGGCTGCTAAGGGACCTCATTGATAAGCAGACATG  
GACAGACGAGGGCTCAGTCTCAGAGCAAATGCTGCGGAGTGAACACTACTCCTCGCCTGTG  
TGCACAACTATCAGCCGTGCGTACAGAGGGCAGAAGGCTATTTCAAGAAAGTGAAGGAATCC  
AATGGAACTTTGAGCCTGCCTGTGACGTCAGCTTGGCAGTGTGTTGCTGTGGGGGGCCAGAG  
CACAGAAGGCTGGGATTTTCTTTATAGTAAATATCAGTTTCTTTGTCCAGTACTGAGAAAA  
GCCAAATTGAATTTGCCCTCTGCAGAACCCAAAATAAGGAAAAGCTTCAATGGCTACTAGAT  
GAAAGCTTTAAGGGAGATAAAATAAAAACTCAGGAGTTTCCACAAATTTTACACTCATTGG  
CAGGAACCCAGTAGGATACCCACTGGCCTGGCAATTTCTGAGGAAAACTGGAACAACTTG  
TACAAAAGTTTGAACCTGGCTCATCTTCATAGCCCATGGTAATGGGTACAACAAATCAA  
TTCTCCACAAGAACACGGCTTGAAGAGGTAAGGATTCTTCAGCTCTTTGAAAGAAAATGG  
TTCTCAGCTCCGTTGTGTCCAACAGACAATTGAAACCATTGAAGAAAACATCGGTTGGATGG  
ATAAGAATTTTGATAAAATCAGAGTGTGGCTGCAAAGTGAAAAGCTTGAACGTATGTAAAAA  
TTCTCCTCCCTTGCCCGGTTCTGTATCTCTAATCACCACATTTTGTGAGTGTATTTTCAA  
ACTAGAGATGGCTGTTTTGGCTCCAAGTGGAGATACTTTTTTCCCTTCAACTCATTTTTTGA  
CTATCCCTGTGAAAAGAATAGCTGTAGTTTTTTCATGAATGGGCTTTTTTCATGAATGGGCTA  
TCGCTACCATGTGTTTTGTTTCATCAGGTGTGGCTGCAACGTAAACCCCAAGTGTGGGT  
TCCCTGCCACAGAAGAATAAAGTACCTTATTCTCTCAAAAAAAAAAAAAAAAAAAAAAAAAA

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FIGURE 248

MVFLPLKWSLATMSFLLSSLLALLTVSTPSWCQSTEASPKRSDGTPFPWNKIRLPEYVIPVH  
YDLLIHANLTTLTFWGTTKVEITASQPTSTIILHSHHLQISRATLRKGAGERLSEEPLOVLE  
HPPQEQIALLAPEPLLVLGPLYTVVIHYAGNLSETFHGFYKSTYRTKEGELRILASTQFEPTA  
ARMAFPCFDEPAFKASFSIKIRREPRHLAISNMPLVKSVTVAEGLIEDHFDVTVKMSTYLVA  
FIISDFESVKITKSGVKVSVYAVPDKINQADYALDAAVTLLFEFYEDYFSIPYPLPKQDLAA  
IPDFQSGAMENWGLTTYRESALLFDAEKSSASSKLGITVTVAHELAHQWFGNLVTMEWWNDL  
WLNEGFAKFMFVSVSVTHPELKVG DYFFGKCFDAMEVDALNSSHPVSTPVENPAQIREMFD  
DVSYDKGACILNMLREYLSADAFKSGIVQYLQKHSYKNTKNEDLWDSMASICPTDGVKGMDG  
FCSRSQHSSSSSHWHQEGVDVKTMMNTWTLQRGFPLITITVRGRNVHMKQEHYMKGSDGAPD  
TGYLWHVPLTFITSKSNMVHRFLLKTKTDVLILPEEVEWIKFNVGMNGYYIVHYEDDGWDSL  
TGLLKGTHTAVSSNDRASLINNAFQLV SIGKLSIEKALDLSLYLKHETEIMPVFQGLNELIP  
MYKLMKSRDMNEVETQFKAFILRLRLDLIDKQTTWTDEGSVSEQMLRSELLLLACVHNYQPCV  
QRAEGYFRKWKESNGNLSLPVDVTLAVFAVGAQSTEGWDFLYSKYQFSLSTEKSQIEFALC  
RTQNKEKLQWLLDESFGDKIKTQEFPPQILTLIGRNPVGYPLAWQFLRKNWNKLQKFELGS  
SSIAHVMGTTNQFSTRTRLEEVKGFFSSLKENGSQLRCVQQT IETIEENIGWMDKNFDKIR  
VWLQSEKLERM

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FIGURE 249

CAGCCACAGACGGGTCATGAGCGCGGTATTACTGCTGGCCCTCCTGGGGTTCATCCTCCAC  
TGCCAGGAGTGCAGGCGCTGCTCTGCCAGTTTGGGACAGTTCAGCATGTGTGGAAGGTGTCC  
GACCTACCCCGGCAATGGACCCCTAAGAACACCAGCTGCGACAGCGGCTTGGGGTGCCAGGA  
CACGTTGATGCTCATTGAGAGCGGACCCCAAGTGAGCCTGGTGCTCTCCAAGGGCTGCACGG  
AGGCCAAGGACCAGGAGCCCCGCGTCACTGAGCACCGGATGGGCCCCGGCCTCTCCCTGATC  
TCCTACACCTTCGTGTGCCGCCAGGAGGACTTCTGCAACAACCTCGTTAACTCCCTCCCGCT  
TTGGGCCCCACAGCCCCCAGCAGACCCAGGATCCTTGAGGTGCCAGTCTGCTTGTCTATGG  
AAGGCTGTCTGGAGGGGACAACAGAAGAGATCTGCCCCAAGGGGACCACACTGTTATGAT  
GGCCTCCTCAGGCTCAGGGGAGGAGGCATCTTCTCCAATCTGAGAGTCCAGGGATGCATGCC  
CCAGCCAGGTTGCAACCTGCTCAATGGGACACAGGAAATTGGGCCCCGTGGGTATGACTGAGA  
ACTGCAATAGGAAAGATTTTCTGACCTGTTCATCGGGGACCACCATTATGACACACGGAAAC  
TTGGCTCAAGAACCCACTGATTGGACCACATCGAATACCGAGATGTGCGAGGTGGGGCAGGT  
GTGTGAGGAGACGCTGCTGCTCATAGATGTAGGACTCACATCAACCCTGGTGGGGACAAAAG  
GCTGCAGCACTGTTGGGGCTCAAAATTCCCAGAAGACCACCATCCACTCAGCCCCCTCCTGGG  
GTGCTTGTGGCCTCCTATACCCACTTCTGCTCCTCGGACCTGTGCAATAGTGCCAGCAGCAG  
CAGCGTTCTGCTGAACTCCCTCCCTCCTCAAGCTGCCCCCTGTCCAGGAGACCGGCAGTGTC  
CTACCTGTGTGCAGCCCCCTTGGAACCTGTTCAAGTGGCTCCCCCGAATGACCTGCCCCAGG  
GGCGCCACTCATTGTTATGATGGGTACATTCATCTCTCAGGAGGTGGGCTGTCCACCAAAAT  
GAGCATTACAGGGCTGCGTGGCCCAACCTTCCAGCTTCTTGTGAACCACACCAGACAAATCG  
GGATCTTCTCTGCGCGTGAGAAGCGTGATGTGCAGCCTCCTGCCTCTCAGCATGAGGGAGGT  
GGGGCTGAGGGCCTGGAGTCTCTCACTTGGGGGGTGGGGCTGGCACTGGCCCCAGCGCTGTG  
GTGGGGAGTGGTTTGCCCTTCCCTGCTAACTCTATTACCCCCACGATTCTTCACCGCTGCTGA  
CCACCCACACTCAACCTCCCTCTGACCTCATAACCTAATGGCCTTGACACCAGATTCTTTC  
CCATTCTGTCCATGAATCATCTTCCCCACACACAATCATTATCTACTCACCTAACAGCA  
ACACTGGGGAGAGCCTGGAGCATCCGGACTTGCCCTATGGGAGAGGGGACGCTGGAGGAGTG  
GCTGCATGTATCTGATAATACAGACCCTGTCCTTTCA

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FIGURE 250

MSAVLLALLGFILPLPGVQALLCQFGTVQHVKVSDLPRQWTPKNTSCDSGLGCQDTLMLI  
ESGPQVSLVLSKGCTEAKDQEPRVTEHRMGPGLSLISYTFVCRQEDFCNNLVNSLPLWAPQP  
PADPGSLRCPVCLSMEGCLEGTTEEICPKGTTHCYDGLLRRLRGGGIFSNLRVQGCMPPQPGCN  
LLNGTQEIGPVGMTENCNRKDFLTCHRGTTIMTHGNLAQEPTDWTTSNTEMCEVGQVCQETL  
LLIDVGLTSTLVGTKGCSTVGAQNSQKTTIHSAPPGVLVASYTHFCSSDLCNSASSSSVLLN  
SLPPQAAPVPGDRQCPTCVQPLGTCSSGSPRMTCPRGATHCYDGYIHLGGGLSTKMSIQGC  
VAQPSSFLLNHTRQIGIFSAREKRDVQPPASQHEGGGAEGLESLTWGVGLALAPALWWGVVCPSC

FIGURE 251

CCGACGGGCAGGACGCCCCGTTGCGCTAGCGCGTGCTCAGGAGTTGGTGTCTCTGCCTGCGCT  
CAGGATGAGGGGGAATCTGGCCCTGGTGGGCGTTCTAATCAGCCTGGCCTTCCTGTCACTGCTG  
CCATCTGGACATCCTCAGCCGGCTGGCGATGACGCCTGCTCTGTGCAGATCCTCGTCCCTGG  
CCTCAAAGGGGATGCGGGAGAGAAGGGAGACAAAGGCGCCCCGGACGGCCTGGAAGAGTCG  
GCCCCACGGGAGAAAAAGGAGACATGGGGGACAAAGGACAGAAAGGCAGTGTGGGTCGTCTCAT  
GGAAAAATTGGTCCCATTGGCTCTAAAGGTGAGAAAGGAGATTCCGGTGACATAGGACCCCC  
TGGTCCTAATGGAGAACCAGGCCTCCCATGTGAGTGACGCCAGCTGCGCAAGGCCATCGGGG  
AGATGGACAACCAGGTCTCTCAGCTGACCAGCGAGCTCAAGTTCATCAAGAATGCTGTGCGC  
GGTGTGCGCGAGACGGAGAGCAAGATCTACCTGTGGTGAAGGAGGAGAAGCGCTACGCGGA  
CGCCCAGCTGTCTGCCAGGGCCGCGGGGGCACGCTGAGCATGCCCAAGGACGAGGCTGCCA  
ATGGCCTGATGGCCGCATACCTGGCGCAAGCCGGCCTGGCCCCGTGTCTTCATCGGCATCAAC  
GACCTGGAGAAGGAGGGCGCCTTCGTGTACTCTGACCACTCCCCCATGCGGACCTTCAACAA  
GTGGCGCAGCGGTGAGCCCAACAATGCCTACGACGAGGAGGACTGCGTGGAGATGGTGGCCT  
CGGGCGGCTGGAACGACGTGGCCTGCCACACCACCATGTACTTCATGTGTGAGTTTGACAAG  
GAGAACATGTGAGCCTCAGGCTGGGGCTGCCCCATTGGGGGGCCCCACATGTCCCTGCAGGGTT  
GGCAGGGACAGAGCCCAGACCATGGTGCCAGCCAGGGAGCTGTCCCTCTGTGAAGGGTGGAG  
GCTCACTGAGTAGAGGGCTGTTGTCTAAACTGAGAAAATGGCCTATGCTTAAGAGGAAAATG  
AAAGTGTTCTGGGGTGCTGTCTCTGAAGAAGCAGAGTTTCATTACCTGTATTGTAGCCCCA  
ATGTCATTATGTAATTATTACCCAGAATTGCTCTTCCATAAAGCTTGTGCCTTTGTCCAAGC  
TATACAATAAAATCTTTAAGTAGTGAGTAGTTAAGTCCAAAAAAAAAAAAAAAAAAAAA



FIGURE 252

M R G N L A L V G V L I S L A F L S L L P S G H P Q P A G D D A C S V Q I L V P G L K G D A G E K G D K G A P G R P G R V G  
P T G E K G D M G D K G Q K G S V G R H G K I G P I G S K G E K G D S G D I G P P G P N G E P G L P C E C S Q L R K A I G E  
M D N Q V S Q L T S E L K F I K N A V A G V R E T E S K I Y L L V K E E K R Y A D A Q L S C Q G R G G T L S M P K D E A A N  
G L M A A Y L A Q A G L A R V F I G I N D L E K E G A F V Y S D H S P M R T F N K W R S G E P N N A Y D E E D C V E M V A S  
G G W N D V A C H T T M Y F M C E F D K E N M

FIGURE 253

AGTGACTGCAGCCTTCCTAGATCCCCCTCCACTCGGTTTCTCTCTTTGCAGGAGCACCGGCAG  
CACCAGTGTGTGAGGGGAGCAGGCAGCGGTCTAGCCAGTTCCTTGATCCTGCCAGACCACC  
CAGCCCCCGGCACAGAGCTGCTCCACAGGCACCATGAGGATCATGCTGCTATTACAGCCAT  
CCTGGCCTTCAGCCTAGCTCAGAGCTTTGGGGCTGTCTGTAAGGAGCCACAGGAGGAGGTGG  
TTCCTGGCGGGGGCCGCAGCAAGAGGGATCCAGATCTCTACCAGCTGCTCCAGAGACTCTTC  
AAAAGCCACTCATCTCTGGAGGGATTGCTCAAAGCCCTGAGCCAGGCTAGCACAGATCCTAA  
GGAATCAACATCTCCCGAGAAACGTGACATGCATGACTTCTTTGTGGGACTTATGGGCAAGA  
GGAGCGTCCAGCCAGAGGGAAAGACAGGACCTTTCTTACCTTCAGTGAGGGTTCCTCGGCCC  
CTTCATCCCAATCAGCTTGGATCCACAGGAAAGTCTTCCCTGGGAACAGAGGAGCAGAGACC  
TTTATTAAGACTCTCCTACGGATGTGAATCAAGAGAACGTCCCCAGCTTTGGCATCCTCAAGT  
ATCCCCCGAGAGCAGAATAGGTACTCCACTTCCGGACTCCTGGACTGCATTAGGAAGACCTC  
TTTCCCTGTCCCAATCCCCAGGTGCGCACGCTCCTGTTACCCTTTCTCTTCCCTGTTCTTGT  
AACATTCTTGCTTTGACTCCTTCTCCATCTTTTCTACCTGACCCTGGTGTGGAAACTGCA  
TAGTGAATATCCCCAACCCCAATGGGCATTGACTGTAGAATACCCTAGAGTTCCTGTAGTGT  
CCTACATTAAAAATATAATGTCTCTCTCTATTCTCAACAATAAAGGATTTTGCATATGAA  
AA

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FIGURE 254

MRIMLLFTAILAFSLAQSFQAVCKEPQEEVVPGGGRSKRDPDLYQLLQRLFKSHSSLEGLLK  
ALSQASTDPKESTSPEKRDMDHDFVGLMGKRSVQPEGKTGPFPLPSVRVPRPLHPNQLGSTGK  
SSLGTEEQRPL

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FIGURE 255

GGGCGTCTCCGGCTGCTCCTATTGAGCTGTCTGCTCGCTGTGCCCCTGTGCCTGCTGTGCC  
CGCGCTGTGCGCGCTGCTACCGCGTCTGCTGGACGCGGGAGACGCCAGCGAGCTGGTGATTG  
GAGCCCTGCGGAGAGCTCAAGCGCCCAGCTCTGCCCCAGGAGCCCAGGCTGCCCCGTGAGTC  
CCATAGTTGCTGCAGGAGTGGAGCCATGAGCTGCGTCCTGGGTGGTGTATCCCCCTTGGGGC  
TGCTGTTCTGCTGCTGCGGATCCCAAGGCTACCTCCTGCCCAACGTCACTCTCTTAGAGGAG  
CTGCTCAGCAAATACCAGCACAAACGAGTCTCACTCCCGGGTCCGCAGAGCCATCCCCAGGGA  
GGACAAGGAGGAGATCCTCATGCTGCACAACAAGCTTCGGGGCCAGGTGCAGCCTCAGGCCT  
CCAACATGGAGTACATGGTGAGCGCCGGCTCCGGCCGCAGAGGCTGGCACCGGGGGTGGGGC  
CTGGGCCACCCAGCCTGCTCTGTTCCCCAGCCAGCTCTGTTCCCCAGCCAGTGCGTGTGATGG  
CTGGCTCAGGGTCTCCTCTGGCAGGGGAGGATCCCGGCTCTGTTCTGTTTTGTTTGTGTTGTT  
TTGAGACAGGGTCTCACTCTGCCACTGACGCTGGAGTGCAATGGCACAATCGTCATGCCCTG  
AAACCTTAGACTCCCGGGGTAAAGCGATCCTGCTTCAGCCTCCCAAGTAGCTGGAACTACAG  
GCATGCACCATGGTGCCCAGCTAGATTTTAAATATTTTGTGGAGATGGGGGTCTTGCTACGT  
TGCCCAGGCTGGTCTTGAACTCCTAGGCTCAAGCAATCCTCCTGCCTCAGCCTCTCAAAGTG  
CTAGGATTATAGGCATGAGTCACCCTGTCTGGCTCTGGCTCTGTTCTTAACATTCTGCCAAA  
ACAACACACGTGGGTTCCCTGTGCAGAGCCTGCCTCGTTGCCTTCATGTCACTCTTGGTAGC  
TCCACTGGGAACACAGCTCTCAGCCTTTCCACCTGGAGGCAGAGTGGGGAGGGGGCCAGGG  
CTGGGCTTTGCTGATGCTGATCTCAGCTGTGCCACACGCTAGCTGCACCACCCTGACTTCTC  
CTTAGCCCCGTGTGAGCCTCACTTTCCACTTGGAGAGTCCTTCCTCGCGTGCGTGGCATGACT  
GTGAGATAAGTCGAGGCTGTGAAGGGCCCGGCACAGACTGACCTGCCTCCCCAACCCCTAGG  
CTTTGCTAACCGGGAAAGGAGCTAACGGTGACAGAAGACAGCCAAGGTCAACCCTCCCGGGT  
GATTGTGATGGGTGTTCCAGGTGTGGTTGGGCGATGCTGCTACTTGACCCCAAGCTCCAGTG  
TGGAACCTTCCTTCCTGGCTGGTTTTCCAGAACTACAGAGGAATGGACCACAGTCTTCCAGG  
GTCCCTCCTCGTCCACCAACCGGGAGCCTCCACCTTGGCCATCCGTGAGCTATGAATGGCTT  
TTTAAACAAACCCACGTCCCAGCCTGGGTAACATGGTAAAGCCCCGTCTCTACAAAAAAATC  
CAAGTTAGCCGGGCATGGTGGTGCGCACCTGTAGTCCCAGCTGCAGTGGGACTGAGGTGGAG  
GTGGAGGTGGGGGTGGGAGCTGAGGAAGGAGGATCGCTTGAGCCTGGGAAGTCGAGGCTGC  
AGTGAGCTGAGATTGCACCACTGCACTCCAGCCTGGGTGACAGAGCAAGACCCTGTCTCAAAA

FIGURE 256

MSCVLGGV IPLGLLFLVCGSQGYLLPNVTLLLEELLSKYQHNEHSRVRRAIPREDKEEILML  
HNKLRGQVQPQASNMEYMVSAAGSGRRGWHRGWGLGHQPALFPSQLCSPASACDGLRVSSGR  
GGSRLCSVLFVCFETGSHSATDAGVQWHNRHALKP

FIGURE 257

AAGGAGAGGCCACCGGGACTTCAGTGTCTCCTCCATCCCAGGAGCGCAGTGGCCACTATGGG  
GTCTGGGCTGCCCCCTTGTCCTCCTCTTGACCCTCCTTGGCAGCTCACATGGAACAGGGCCGG  
GTATGACTTTGCAACTGAAGCTGAAGGAGTCTTTTCTGACAAATTCCTCCTATGAGTCCAGC  
TTCCTGGAATTGCTTGAAAAGCTCTGCCTCCTCCTCCATCTCCCTTCAGGGACCAGCGTCAC  
CCTCCACCATGCAAGATCTCAACACCATGTTGTCTGCAACACATTGACAGCCATTGAAGCCTG  
TGTCTTCTTGCCCCGGGCTTTTGGGCCGGGGATGCAGGAGGCAGGCCCCGACCCTGTCTTT  
CAGCAGGCCCCCACCTCCTGAGTGGCAATAAATAAAATTCGGTATGCTG

FIGURE 258

MSGGLPLVLLLTLLGSSHGTGPGMTLQLKLKESFLTNSSESSFLELLEKLCLLLHLPSTG  
VTLHHARSQHHVVCNT

FIGURE 259

AATTGTATCTGTGTAATGTTAAAAACAAACGAAATAAAATAGAAGGAAAACTTTCTGAGTTT  
CAAAAAACAACAGACTAGTACTCTAAAGAACTCTTTAAAAACAATTAACTGTTAGGATTGCAGT  
TATGATTGGATATTATTTAATTCTGTTTCTGATGTGGGGTTCCTCCACTGTGTTCTGTGTGC  
TATTAATATTTACCATTGCAGAAGCTTCATTCACTGTTGAAAAATGAATGCTTAGTGGATCTG  
TGCCTCTTACGCATATGTTACAAATTATCTGGAGTTCCTAATCAATGCAGAGTTCCCCTCCC  
CTCCGATTGTTCTAAATTAATTGAAAGATGTCTGCTGTGGAAAAAGGCATGTATTTAAATCTG  
TATGATTCTCAACCATCTTTAGTTGGGAAAGGTCCTTGAAAGCCAATGGAAATACTTTTTTTT  
TTTTCTTGGCACTAATCAAGTGAGTGTTACCTTTTCACTTAGTAGGATGTGTTGTTACGCTA  
GTAAAATAGAAACCTGTGTTTATTCTCAGGTATTTTAGAAACAACAGCCATCATTTTATTTT  
ATGTGTGTGTTCTTGGCTGTATTCATAAATTATATATTTTTGGGCTATCAAATATTACTTCAT  
TCAATATAAATAACAATAGTAGAAGTTGTTTACTTAGATATGCTTTCTAGTTGCATTTTCTC  
AGCCTATGTAAGACTACTTTGTTGTAATAGCCTTTGAAATTTACAGTACTGTCTCTCTACTA  
TCTTCAGATTACTTGATTCAAATAAACCAATTATGTTTGTAATTGATATTAATAAAACCAGA  
ATAAAAGTTCATATCTACCC



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FIGURE 260

MIGYYLILFLMWGSSTVFCVLLIFTIAEASFVENECLVDLCLLRICYKLSGVPNQCRVPLP  
SDCSK

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FIGURE 261

GAGGATTTGCCACAGCAGCGGATAGAGCAGGAGAGCACCAACCGGAGCCCTTGAGACATCCTT  
GAGAAGAGCCACAGCATAAGAGACTGCCCTGCTTGGTGTGTTTTGCAGGATGATGGTGGCCCTT  
CGAGGAGCTTCTGCATTGCTGGTTCTGTTCCCTTGACAGCTTTTCTGCCCCCGCCGAGTGTAC  
CCAGGACCCAGCCATGGTGCATTACATCTACCAGCGCTTTCGAGTCTTGGAGCAAGGGCTGG  
AAAAATGTACCCAAGCAACGAGGGCATACATTCAAGAATTCCAAGAGTTCTCAAAAAATATA  
TCTGTTCATGCTGGGAAGATGTGAGACCTACACAAAGTGAGTACAAGAGTGCAGTGGGTAACCTT  
GGCACTGAGAGTTGAACGTGCCAACGGGAGATTGACTACATACAATACCTTCGAGAGGGCTG  
ACGAGTGCATCGTATCAGAGGACAAGACACTGGCAGAAATGTTGCTCCAAGAAGCTGAAGAA  
GAGAAAAAGATCCGGACTCTGCTGAATGCAAGCTGTGACAACATGCTGATGGGCATAAAGTC  
TTTGAAAATAGTGAAGAAGATGATGGACACACATGGCTCTTGGATGAAAGATGCTGTCTATA  
ACTCTCCAAAGGTGTACTTATTAATTGGATCCAGAAACAACACTGTTTGGGAATTTGCAAAC  
ATACGGGCATTTCATGGAGGATAACACCAAGCCAGCTCCCCGGAAGCAAATCCTAACACTTTC  
CTGGCAGGGAACAGGCCAAGTGATCTACAAAGGTTTTCTATTTTTTCATAACCAAGCAACTT  
CTAATGAGATAATCAAATATAACCTGCAGAAGAGGACTGTGGAAGATCGAATGCTGCTGCCA  
GGAGGGGTAGGCCGAGCATTTGGTTTTACCAGCACTCCCCCTCAACTTACATTGACCTGGCTGT  
GGATGAGCATGGGCTCTGGGCCATCCACTCTGGGCCAGGCACCCATAGCCATTTGGTTCTCA  
CAAAGATTGAGCCGGGCACACTGGGAGTGGAGCATTTCATGGGATACCCCATGCAGAAGCCAG  
GATGCTGAAGCCTCATTCTCTTGTGTGGGGTTCTCTATGTGGTCTACAGTACTGGGGGCCA  
GGGCCCTCATCGCATCACCTGCATCTATGATCCACTGGGCACTATCAGTGAGGAGGACTTGC  
CCAACTTGTTCTTCCCCAAGAGACCAAGAAGTCACTCCATGATCCATTACAACCCAGAGAT  
AAGCAGCTCTATGCCTGGAATGAAGGAAACCAGATCATTTACAAACTCCAGACAAAGAGAAA  
GCTGCCTCTGAAGTAATGCATTACAGCTGTGAGAAAGAGCACTGTGGCTTTGGCAGCTGTTCT  
TACAGGACAGTGAGGCTATAGCCCCTTCACAAATATAGTATCCCTCTAATCACACACAGGAAG  
AGTGTGTAGAAGTGGAATACGTATGCCTCCTTTCCCAAATGTCAGTGCCTTAGGTATCTTC  
CAAGAGCTTAGATGAGAGCATATCATCAGGAAAGTTTCAACAATGTCCATTACTCCCCAAA  
CCTCCTGGCTCTCAAGGATGACCACATTCTGATACAGCCTACTTCAAGCCTTTTGTTTTACT  
GCTCCCCAGCATTTACTGTAACCTCTGCCATCTTCCCTCCCACAATTAGAGTTGTATGCCAGC  
CCCTAATATTACCACTGGCTTTTCTCTCCCCTGGCCTTTGCTGAAGCTCTTCCCTCTTTTT  
CAAATGTCTATTGATATTCTCCCATTTTCACTGCCCAACTAAAATACTATTAATATTTCTTT  
CTTTCTTTTTCTTTTTTTTGAGACAAGGTCTCACTATGTTGCCAGGCTGGTCTCAAACCTCC  
AGAGCTCAAGAGATCCTCCTGCCTCAGCCTCCTAAGTACCTGGGATTACAGGCATGTGCCAC  
CACACCTGGCTTAAAATACTATTTCTTATTGAGGTTTAACCTCTATTTCCCCTAGCCCTGTC  
CTTCCACTAAGCTTGGTAGATGTAATAATAAAGTGAAAATATTAACATTTGAATATCGCTTT  
CCAGGTGTGGAGTGTGTCACATCATTGAATTCTCGTTTTACCTTTGTGAAACATGCACAAG  
TCTTTACAGCTGTCTATTCTAGAGTTTAGGTGAGTAACACAATTACAAAGTGAAAGATACAGC  
TAGAAAATACTACAAATCCCATAGTTTTTCCATTGCCCAAGGAAGCATCAAATACGTATGTT  
TGTTACCTACTCTTATAGTCAATGCGTTTCATCGTTTCAGCCTAAAAATAATAGTCTGTCCC  
TTTAGCCAGTTTTTCATGTCTGCACAAGACCTTTCAATAGGCCTTTCAAATGATAATTCCTCC  
AGAAAACCAGTCTAAGGGTGAGGACCCCAACTCTAGCCTCCTCTGTCTTGTCTGTCTCTGT  
TTCTCTCTTTCTGCTTTAAATTCAATAAAAGTGACACTGAGCAAAAAAAAAAAAAAA

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FIGURE 262

MMVALRGASALLVLFLLAFLPPPQCTQDPAMVHYIYQRFVLEQGLEKCTQATRAYIQEFQE  
FSKNISVMLGRCQTYTSEYKSAVGNLALRVERAQREIDYIQYLREADECIVSEDKTLAEMLL  
QEAEEEKKIRTLLNASCDNMLMGIKSLKIVKKMMDTHGSWMKDAVYNPKVYLLIGSRNNTV  
WEFANIRAFMEDNTKPAPRKQILTLSWQGTGQVIYKGFLFFHNQATSNEIIKYNLQKRTVED  
RMLLPGGVGRALVYQHSPSTYIDLAVDEHGLWAIHSGPGTHSHLVLTKEPGTLGVEHSWDT  
PCRSQDAEASFLLCGVLYVVYSTGGQGPHRITCIYDPLGTISEEDLPNLFFPKRPRSHSMIH  
YNPRDKQLYAWNEGNQIIYKLQTKRKLPLK

FIGURE 263

GGGCGCCCGCTACTCACTAGCTGAGGTGGCAGTGGTTCACCAACATGGAGCTCTCGCAGA  
TGTCGGAGCTCATGGGGCTGTGGGTGTGCTTGGGCTGCTGGCCCTGATGGCGACGGCGGGCG  
GTAGCGCGGGGGTGGCTGCGCGCGGGGGAGGAGAGGAGCGGCCGGCCCGCCTGCCAAAAAGC  
AAATGGATTTCCACCTGACAAATCTTCGGGATCCAAGAAGCAGAAACAATATCAGCGGATTTC  
GGAAGGAGAAGCCTCAACAACACAACCTTCACCCACCGCCTCCTGGCTGCAGCTCTGAAGAGC  
CACAGCGGGAACATATCTTGATGGACTTTAGCAGCAATGGCAAATACCTGGCTACCTGTGC  
AGATGATCGCACCATCCGCATCTGGAGCACCAAGGACTTCCTGCAGCGAGAGCACCGCAGCA  
TGAGAGCCAACGTGGAGCTGGACCACGCCACCCTGGTGGCCTTCAGCCCTGACTGCAGAGCC  
TTCATCGTCTGGCTGGCCAACGGGGACACCCTCCGTGTCTTCAAGATGACCAAGCGGGAGGA  
TGGGGGCTACACCTTCACAGCCACCCAGAGGACTTCCCTAAAAAGCACAAGGCGCCTGTCA  
TCGACATTGGCATTGCTAACACAGGGAAGTTTATCATGACTGCCTCCAGTGACACCACTGTCT  
CTCATCTGGAGCCTGAAGGGTCAAGTGCTGTCTACCATCAACACCAACCAGATGAACAACAC  
ACACGCTGCTGTATCTCCCTGTGGCAGATTTGTAGCCTCGTGTGGCTTCACCCAGATGTGA  
AGGTTTGGGAAGTCTGCTTTGGAAAGAAGGGGGAGTTCCAGGAGGTGGTGGCAGCCTTCGAA  
CTAAAGGGCCACTCCGCGGCTGTGCACTCGTTTGCTTTCTCCAACGACTCACGGAGGATGGC  
TTCTGTCTCCAAGGATGGTACATGGAACTGTGGGACACAGATGTGGAATACAAGAAGAAGC  
AGGACCCCTACTTGCTGAAGACAGGCCGCTTTGAAGAGGCGGCGGGTGCCGCGCCGTGCCGC  
CTGGCCCTCTCCCCAACGCCACAGGTCTTGGCCTTGGCCAGTGGCAGTAGTATTCTCTCTA  
CAATACCCGGCGGGGCGAGAAGGAGGAGTGCTTTGAGCGGGTCCATGGCGAGTGTATCGCCA  
ACTTGTCTTTGACATCACTGGCCGCTTTCTGGCCTCCTGTGGGGACCGGGCGGTGCCGCTG  
TTTCACAACACTCCTGGCCACCGAGCCATGGTGGAGGAGATGCAGGGCCACCTGAAGCGGGC  
CTCCAACGAGAGCACCCGCCAGAGGCTGCAGCAGCAGCTGACCCAGGCCCAAGAGACCCTGA  
AGAGCCTGGGTGCCCTGAAGAAGTGACTCTGGGAGGGCCCGGCGCAGAGGATTGAGGAGGAG  
GGATCTGGCCTCCTCATGGCACTGCTGCCATCTTTCTCCAGGTGGAAGCCTTTCAGAAGG  
AGTCTCCTGGTTTTCTTACTGGTGGCCCTGCTTCTTCCATTGAACTACTCTTGTCTACTT  
AGGTCTCTCTCTTCTTGCTGGCTGTGACTCCTCCCTGACTAGTGGCCAAGGTGCTTTTCTTC  
CTCCAGGCCCAGTGGGTGGAATCTGTCCCCACCTGGCACTGAGGAGAATGGTAGAGAGGAG  
AGGAGAGAGAGAGAGAATGTGATTTTGGCCTTGTTGGCAGCACATCCTCACACCCAAAGAAG  
TTTGTAATGTTCAGAACAACTAGAGAACACCTGAGTACTAAGCAGCAGTTTTGCAAGGA  
TGGGAGACTGGGATAGCTTCCCATCACAGAACTGTGTTCCATCAAAAAGACACTAAGGGATT  
TCCTTCTGGGCCTCAGTTCTATTTGTAAGATGGAGAATAATCCTCTCTGTGAACTCCTTGCA  
AAGATGATATGAGGCTAAGAGAATATCAAGTCCCCAGGTCTGGAAGAAAAGTAGAAAAGAGT  
AGTACTATTGTCCAATGTGATGAAAGTGTTAAAGTGGGAACCAGTGTGCTTTGAAACCAAA  
TTAGAAACACATTCCTTGGGAAGGCAAAGTTTCTGGGACTTGATCATAATTTTATATGGT  
TGGGACTTCTCTCTTCGGGAGATGATATCTTGTTTAAGGAGACCTCTTTTCAGTTCATCAAG  
TTCATCAGATATTGAGTGCCCACTCTGTGCCCAAATAAATATGAGCTGGGGATTAAAAAAA  
AAA

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FIGURE 264

MELSQMSELMGLSVLLGLLALMATAAVARGWLRAGEERSGRPACQKANGFPPDKSSGSKKQK  
QYQIRIRKEKPQHNFTHRLLAAALKSHSGNISCMDFSSNGKYLATCADDRTIRIWSTKDFLQ  
REHRSMRANVELDHATLVRFPDCRAFI VWLANGDTLRVFKMTKREDGGYTFTATPEDFPKK  
HKAPVIDIGIANTGKFIMTASSDTTVLIWSLKGQVLSTINTNQMNNTHAAVSPCGRFVASCG  
FTPDVKVWEVCFGKKGEFQEVVRAFELKGHSAAVHSFAFSNDSRRMASVSKDGTWKLWDTDV  
EYKKKQDPYLLKTGRFEEAAGAAPCRLALSPNAQVLALASGSSIHLYNTRRGEKEECFERVH  
GECIANLSFDITGRFLASCGDRAVRLFHNTPGHRAMVEEMQGHLKRASNESTRQRLQQQLTQ  
AQETLKSLGALKK

FIGURE 265

TGGCCTCCCCAGCTTGCCAGGCACAAGGCTGAGCGGGAGGAAGCGAGAGGCATCTAAGCAGG  
CAGTGTTTTGCCTTTCACCCCAAGTGACCATGAGAGGTGCCACGCGAGTCTCAATCATGCTCC  
TCCTAGTAACTGTGTCTGACTGTGCTGTGATCACAGGGGCTGTGAGCGGGATGTCCAGTGT  
GGGGCAGGCACCTGCTGTGCCATCAGCCTGTGGCTTCGAGGGCTGCGGATGTGCACCCCGCT  
GGGGCGGGAAGGCGAGGAGTGCCACCCCGGCAGCCACAAGGTCCCCTTCTTCAGGAAACGCA  
AGCACACACCTGTCTTGCTTGCCCCAACCTGCTGTGCTCCAGGTTCCCGGACGGCAGGTAC  
CGCTGCTCCATGGACTTGAAGAACATCAATTTTAGGCGCTTGCTGGTCTCAGGATACCCA  
CCATCCTTTTCTGAGCACAGCCTGGATTTTATTTCTGCCATGAAACCCAGCTCCCATGAC  
TCTCCCAGTCCCTACACTGACTACCTGATCTCTTGTCTAGTACGCACATATGCACACAG  
GCAGACATACCTCCCATCATGACATGGTCCCCAGGCTGGCCTGAGGATGTACAGCTTGAGG  
CTGTGGTGTGAAAGGTGGCCAGCCTGGTTCTCTTCCCTGCTCAGGCTGCCAGAGAGGTGGTA  
AATGGCAGAAAGGACATTCCCCCTCCCCTCCCAGGTGACCTGCTCTCTTTCCTGGGCCCTG  
CCCCCTCTCCCCACATGTATCCCTCGGTCTGAATTAGACATTCTGGGCACAGGCTCTTGGGT  
GCATTGCTCAGAGTCCCAGGTCCTGGCCTGACCCTCAGGCCCTTCACGTGAGGTCTGTGAGG  
ACCAATTTGTGGGTAGTTCATCTTCCCTCGATTGGTTAACTCCTTAGTTTTAGACCACAGAC  
TCAAGATTGGCTCTTCCCAGAGGGCAGCAGACAGTCACCCCAAGGCAGGTGTAGGGAGCCCA  
GGGAGGCCAATCAGCCCCCTGAAGACTCTGGTCCCAGTCAGCCTGTGGCTTGTGGCCTGTGA  
CCTGTGACCTTCTGCCAGAATTGTCATGCCTCTGAGGCCCCCTCTTACCACACTTTACCAGT  
TAACCACTGAAGCCCCCAATTTCCACAGCTTTTCCATTAAATGCAAATGGTGGTGGTTCAA  
TCTAATCTGATATTGACATATTAGAAGGCAATTAGGGTGTTCCTTAAACAACCTCCTTTCCA  
AGGATCAGCCCTGAGAGCAGGTGGTGAATTTGAGGAGGGCAGTCCTCTGTCCAGATTGGGG  
TGGGAGCAAGGGACAGGGAGCAGGGCAGGGGCTGAAAGGGGCACTGATTGAGACCAGGGAGG  
CAACTACACACCAACATGCTGGCTTTAGAATAAAAGCACCAACTGAAAAA

FIGURE 266

MKGATRVSIIMLLLVTVSDCAVITGACERDVQCGAGTCCAI SLWLRGLRMCTPLGREGE ECHP  
GSHKVPFFRKRKHHTCPCLPNLLCSRFPDGRYRCSMDLKNINF

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FIGURE 267

AGCGCCCGGGCGTCGGGGCGGTAAAAGGCCGGCAGAAGGGAGGCACTTGAGAAATGTCCTTTC  
CTCCAGGACCCAAGTTTCTTCACCATGGGGATGTGGTCCATTGGTGCAGGAGCCCTGGGGGC  
TGCTGCCTTGGCATTGCTGCTTGCCAACACAGACGTGTTTCTGTCCAAGCCCCAGAAAGCGG  
CCCTGGAGTACCTGGAGGATATAGACCTGAAAACACTGGAGAAGGAACCAAGGACTTTCAAA  
GCAAAGGAGCTATGGGAAAAAATGGAGCTGTGATTATGGCCGTGCGGAGGCCAGGCTGTTT  
CCTCTGTGAGAGGAAGCTGCGGATCTGTCCTCCCTGAAAAGCATGTTGGACCAGCTGGGGC  
TCCCCCTCTATGCAGTGGTAAAGGAGCACATCAGGACTGAAGTGAAGGATTTCCAGCCTTAT  
TTCAAAGGAGAAATCTTCCTGGATGAAAAGAAAAAGTTCTATGGTCCACAAAGGCGGAAGAT  
GATGTTTATGGGATTTATCCGTCTGGGAGTGTGGTACAACTTCTTCCGAGCCTGGAACGGAG  
GCTTCTCTGGAAACCTGGAAGGAGAAGGCTTCATCCTTGGGGGAGTTTTTCGTGGTGGGATCA  
GGAAAGCAGGGCATTCTTCTTGAGCACCGAGAAAAAGAATTTGGAGACAAAGTAAACCTACT  
TTCTGTTCTGGAAGCTGCTAAGATGATCAAACCACAGACTTTGGCCTCAGAGAAAAAATGAT  
TGTGTGAAACTGCCCAGCTCAGGGATAACCAGGGACATTACCTGTGTTTCATGGGATGTATT  
GTTTCCACTCGTGTCCCTAAGGAGTGAGAAACCCATTTATACTCTACTCTCAGTATGGATTA  
TTAATGTATTTTAATATTCTGTTTAGGCCCCTAAGGCAAAATAGCCCCAAAACAAGACTGA  
CAAAAATCTGAAAAACTAATGAGGATTATTAAGCTAAAACCTGGGAAATAGGAGGCTTAAAA  
TTGACTGCCAGGCTGGGTGCAGTGGCTCACACCTGTAATCCCAGCACTTTGGGAGGCCAAGG  
TGAGCAAGTCACTTGAGGTTCGGGAGTTTCGAGACCAGCCTGAGCAACATGGCGAAACCCGTC  
TCTACTAAAAATACAAAAATCACCCGGGTGTGGTGGCAGGCACCTGTAGTCCCAGCTACCCG  
GGAGGCTGAGGCAGGAGAATCACTTGAACCTGGGAGGTGGAGGTGCGGTGAGCTGAGATCA  
CACCACTGTATTCCAGCCTGGGTGACTGAGACTCTAACTAA



FIGURE 268

MSFLQDPSFFTGMWSIGAGALGAAALALLLANTDVFLSKPQKALEYLEDIDLKTLEKEPR  
TFKAKELWEKNGAVIMAVRRPGCFLCREEAADLSSLKSMLDQLGVPLYAVVKEHIRTEVKDF  
QPYFKGEIFLDEKKKFYGPQRRKMMFMGFIRLGWYNFFRAWNGGFSGNLEGEFGFILGGVFV  
VGSGKQGILLEHREKEFGDKVNLLSVLEAAKMIKPQTLASEKK

FIGURE 269

ACGGACCGAGGGTTCGAGGGAGGGACACGGACCAGGAACCTGAGCTAGGTCAAAGACGCCCCG  
GGCCAGGTGCCCCGTGCGAGGTGCCCCCTGGCCGGAGATGCGGTAGGAGGGGCGAGCGCGAGA  
AGCCCCCTTCCTCGGCGCTGCCAACCCGCCACCCAGCCCATGGCGAACCCCGGGCTGGGGCTG  
CTTCTGGCGCTGGGCCTGCCGTTCTGCTGGCCCCTGGGGCCGAGCCTGGGGGCAAATACA  
GACCACTTCTGCAAATGAGAATAGCACTGTTTTGCCTTCATCCACCAGCTCCAGCTCCGATG  
GCAACCTGCGTCCGGAAGCCATCACTGCTATCATCGTGGTCTTCTCCCTCTTGGCTGCCTTG  
CTCCTGGCTGTGGGGCTGGCACTGTTGGTGCGGAAGCTTCGGGAGAAGCGGCAGACGGAGGG  
CACCTACCGGCCCAGTAGCGAGGAGCAGTTCTCCCATGCAGCCGAGGCCCGGGCCCCCTCAGG  
ACTCCAAGGAGACGGGTGCAGGGCTGCCTGCCCATCTAGGTCCCCTCTCCTGCATCTGTCTCC  
CTTCATTGCTGTGTGACCTTGGGGAAAGGCAGTGCCCTCTCTGGGCAGTCAGATCCACCCAG  
TGCTTAATAGCAGGGAAGAAGGTACTTCAAAGACTCTGCCCCCTGAGGTCAAGAGAGGATGGG  
GCTATTCACTTTTATATATTTATATAAAATTAGTAGTGAGATGTAAAAAAAAAAAAAAAAAAAA

FIGURE 270

MANPGLGLLLALGLPFLLARWGRAWGQIQTTSANENSTVLPSTSSSSDGNLRPEAITAIIV  
VFSLLAALLLAVGLALLVRKLREKRQTEGTYRPSSEEQFSHAAEARAPQDSKETVQGCLPI

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FIGURE 271

AATATATCATCTATTTATCATTAAATCAATAATGTATTCTTTTATTCCAATAACATTTGGGTT  
TTGGGATTTTAATTTTCAAACACAGCAGAAATGACATTTTTCTGTCACTATTATTATTGTTG  
GTATGTGAAGCTATTTGGAGATCCAATTCAGGAAGCAACACATTGGAGAATGGCTACTTTCT  
ATCAAGAAATAAAGAGAACCACAGTCAACCCACACAATCATCTTTAGAAGACAGTGTGACTC  
CTACCAAAGCTGTCAAAACCACAGGCAAGGGCATAGTTAAAGGACGGAATCTTGACTCAAGA  
GGGTTAATTCTTGGTGCTGAAGCCTGGGGCAGGGGTGTAAAGAAAAACACTTAGATTCAATG  
ATTGTAAATTTAAGGCAAATACACATATTAGTATTACCTTAGTGTAATGTATCCCTGTCATA  
TATACAATAAGGTGAAATTATAAGTACCCATATGCAGTTGGCTGGACAGTTCTAAATTGGACT  
TTATTAATTTTAAAATCAGTAACTGATTTATCACTGGCTATGTGCTTAGATCTACAGGAGA  
TCATATAATTTGATACAAATAAAAGAAAAGTGTCTCTCCCCTTACAGAATTGACATTTTAA  
ATGCGATACAGTTAGAATAGGAAATATGACATTAGAAAGGAAGAATGACAGGGAGAAAGGAA  
AGAAGGGAAAATGTTGCCAAGGAAAAAAA

FIGURE 272

MTFFLSLLLLLVCEAIWRSNSGSNTLENGYFLSRNKENHSQPTQSSLEDSVTPTKAVKTTGK  
GIVKGRNLDSRGLILGAEAWGRGVKKNT

## FIGURE 273

GCCAGGAATAACTAGAGAGGAACAATGGGGTTATTTCAGAGGTTTTGTTTTCTCTTAGTTCT  
GTGCCTGCTGCACCAGTCAAATACCTTCCTTCATTAAGCTGAATAATAATGGCTTTGAAGATA  
TTGTCAATTGTTATAGATCCTAGTGTGCCAGAAGATGAAAAAATAATTGAACAAATAGAGGAT  
ATGGTGACTACAGCTTCTACGTACCTGTTTGAAGCCACAGAAAAAAGATTTTTTTTTCAAAAA  
TGATCTATATTAATTCCTGAGAAATTGGAAGGAAAAATCCTCAGTACAAAAGGCCAAAACATG  
AAAACCATAAACATGCTGATGTTATAGTTGCACCACCTACACTCCCAGGTAGAGATGAACCA  
TACACCAAGCAGTTTACAGAATGTGGAGAGAAAGGCGAATACATTCACCTTCACCCCTGACCT  
TCTACTTGGAAAAAACAATGAATATGGACCACCAGGCAAACTGTTTGTCCATGAGTGGG  
CTCACCTCCGGTGGGGAGTGTGTTGATGAGTACAATGAAGATCAGCCTTTCTACCGTGCTAAG  
TCAAAAAAATCGAAGCAACAAGGTGTTCCGCAGGTATCTCTGGTAGAAATAGAGTTTATAA  
GTGTCAAGGAGGCAGCTGCTTTAGTAGAGCATGCAGAAATTGATTCTACAACAAAACGTATG  
GAAAAGATTGTCAATTCTTTCTGATAAAGTACAAACAGAAAAAGCATCCATAATGTTTATG  
CAAAGTATTGATTCTGTTGTTGAATTTTGTAAACGAAAAAACCCATAATCAAGAAGCTCCAAG  
CCTACAAAACATAAAGTGCAATTTTAGAAGTACATGGGAGGTGATTAGCAATTCTGAGGATT  
TTAAAAACACCATACCCATGGTGACACCACCTCCTCCACCTGCTCTTCATTGCTGAAGATC  
AGTCAAAGAATTGTGTGCTTAGTTCTTGATAAGTCTGGAAGCATGGGGGGTAAGGACCGCCT  
AAATCGAATGAATCAAGCAGCAAAACATTTCTGCTGCAGACTGTTGAAAATGGATCTCCGG  
TGGGGATGGTTCACTTTGATAGTACTGCCACTATTGTAAATAAGCTAATCCAAATAAAAAAGC  
AGTGATGAAAGAAACACACTCATGGCAGGATTACCTACATATCCTCTGGGAGGAACCTCCAT  
CTGCTCTGGAATTAATATGCATTTTCAGGTGATTGGAGAGCTACATTCCTCAACTCGATGGAT  
CCGAAGTACTGCTGCTGACTGATGGGGAGGATAACACTGCAAGTTCTTGATTGATGAAGTG  
AAACAAAGTGGGGCCATTGTTTCATTTTATTGCTTTTGGGAAGAGCTGCTGATGAAGCAGTAAAT  
AGAGATGAGCAAGATAACAGGAGGAAGTCATTTTTATGTTTCAGATGAAGCTCAGAACAATG  
GCCTCATTGATGCTTTTGGGGCTCTTACATCAGGAAATACTGATCTCTCCAGAAAGTCCCTT  
CAGCTCGAAAGTAAGGGATTAACTACTGAATAGTAATGCCTGGATGAACGACACTGTATAAT  
TGATAGTACAGTGGGAAGGACACGTTCTTTCTCATCACATGGAACAGTCTGCCCTCCAGTA  
TTTCTCTCTGGGATCCCAGTGGGAACAATAATGGAAAAATTTACAGTGGATGCAACTTCCAAA  
ATGGCCTATCTCAGTATTCAGGAACCTGCAAAGGTGGGCACCTGGGCATACAATCTTCAAGC  
CAAAGCGAACCCAGAAACATTAACATTTACAGTAACCTCTCGAGCAGCAAAATCTTCTGTGC  
CTCCAATCACAGTGAATGCTAAAAATGAATAAGGACGTAAACAGTTTCCCAGCCCAATGATT  
GTTTACGCAGAAATCTACAAGGATATGTACCTGTTCTTGAGCCAAATGTGATGCTTTTCAT  
TGAATCACAGAAATGGACATACAGAAGTTTTTGGAACTTTTGGATAATGGTGCAGGCGCTGATT  
CTTTCAAGAATGATGGAGTCTACTCCAGGTATTTTACAGCATATACAGAAAATGGCAGATAT  
AGCTTAAAAGTTCCGGCTCATGGAGGAGCAAACTGCCAGGCTAAAAATTACGGCCTCCACT  
GAATAGAGCCGCTACATACCAGGCTGGGTAGTGAACGGGGAATTTGAAGCAAACCCGCCAA  
GACCTGAAATTGATGAGGATACTCAGACCACCTTGGAGGATTTAGCCGAACAGCATCCGGA  
GGTGCAATTTGTGGTATCACAAGTCCCAAGCCTTCCCTTGCCTGACCAATACCCACCAAGTCA  
AATCACAGACCTTGATGCCACAGTTCATGAGGATAAGATTATTCTTACATGGACAGCACCAG  
GAGATAATTTTGTGTTGGAAAAGTTCAACGTTATATCATAAGAATAAGTGCAAGTATTTCTT  
GATCTAAGAGACAGTTTTGATGATGCTCTTCAAGTAAATACTACTGATCTGTCAACAAAGGA  
GGCCAACTCCAAGGAAAAGCTTTGCATTTAAACCAGAAAATATCTCAGAAGAAAATGCAACCC  
ACATATTTTATGCCATTAAAAGTATAGATAAAAGCAATTTGACATCAAAAGTATCCAACATT  
GCACAAGTAACTTTGTTTATCCCTCAAGCAAATCCTGATGACATTGATCCTACACCTACTCC  
TACTCCTACTCCTACTCCTGATAAAAGTCATAATTTCTGGAGTTAATATTTCTACGCTGGTAT  
TGTCTGTGATTGGGTCTGTTGTAATTGTTAACTTTATTTTAAAGTACCACCATTTGAACCTTA  
ACGAAGAAAAAATCTTCAAGTAGACCTAGAAGAGAGTTTTTAAAAAACAACCAATGTAAGT  
AAAGGATATTTCTGAATCTTAAATTCATCCCATGTGTGATCATAACTCATAAAAATAATT  
TTAAGATGTGCGAAAAGGATACTTTGATTAATAAAAAACACTCATGGATATGTA AAAACTGT  
CAAGATTAATAATTAAGTTTCAATTTATTTGTTATTTTATTTGTAAGAAATAGTGATGAAC  
AAAGATCTTTTTCATACTGATACCTGGTTGTATATTATTTGATGCAACAGTTTTCTGAAAT  
GATATTTCAAATTCATCAAGAAATTAATAATCATCTATCTGAGTAGTCAAAATACAAGTAAA  
GGAGAGCAAATAAACACATTTGAAAAA AAAAAAAAAAAAAAAAAAAAAAAAAAAAAA  
AAA

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FIGURE 274

MGLFRGFVFLVLCLLHQSNTSFIKLNNNGFEDIVIVIDPSVPEDEKIIIEQIEDMVTASTY  
LFEATEKRFFFKNVSILIPENWKENPQYKRPKHENHKHADVIVAPPTLPGRDEPYTKQFTEC  
GEKGEYIHFTPDLLLGKKQNEYGPPGKLFVHEWAHLRWGVFDEYNEDQPFYRAKSKKIEATR  
CSAGISGRNRVYKCQGGSCLSRACRIDSTTKLYGKDCQFFPDKVQTEKASIMFMQSIDSVVE  
FCNEKTHNQEAPSLQNIKCNFRSTWEVISNSEDFKNTIPMVTPPPPPVFSLLKISQRIVCLV  
LDKSGSMGGKDRNLNRMNQAAKHFLQTVENGSWVGMVHFDSTATIVNKLIQIKSSDERNTLM  
AGLPTYPLGGTSICSGIKYAFQVIGELHSQLDGSEVLLLLTDGEDNTASSCIDEVKQSGAIVH  
FIALGRAADEAVIEMSKITGGSHFYVSDEAQNNGLIDAFGALTSGNTDLSQKSLQLESKGLT  
LNSNAWMNDTVIIDSTVGKDTFFLITWNSLPPSISLWDPSGTIMENFTVDATSKMAYLSIPG  
TAKVGTWAYNLQAKANPETLTITVTSRAANSSVPPITVNAKMNKDVNSFPSPMIVYAEILQG  
YVPVLGANVTAFIESQNGHTEVLELLDNGAGADSFKNDBGVYSRYFTAYTENGRYSLKVRAHG  
GANTARLKLRPPLNRAAYIPGWVNGEIEANPPRPEIDEDTQTTLEDFSRASGGAFVVSQV  
PSLPLPDQYPPSQITDL DATVHEDKIILTWTPGDNFDVGKVQRYIIRISASILDRLDSFDD  
ALQVNTTDLSPKEANSKESFAFKPENISEENATHIFIAIKSIDKSNLTSKVSANIAQVTLFIP  
QANPDDIDPTPTPTPTPTPKSHNSGVNISTLVLSVIGSVVIVNFILSTTI

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FIGURE 275

CTCCTTAGGTGGAACCCCTGGGAGTAGAGTACTGACAGCAAAGACCGGAAAGACCATACGTCCCCGG  
GCAGGGGTGACAACAGGTGTCTATCTTTTGTATCTCGTGTGTGGCI GCCTTCCTATTTCAAGGAAAGAC  
GCCAAGGTAATTTTGACCCAGAGGAGCAATGATGTAGCCACCTCCFAACCTTCCCTTCTTGAACCCCC  
AGTTATGCCAGGATTTACTAGAGAGTGTCAACTCAACCAGCAAGCGGCTCCTTCGGCTTAACCTTGTGG  
TTGGAGGAGAGAACCTTTGTGGGGCTGCGTTCTCTTAGCAGTGTCTCAGAAGTGAAGTGCCTGAGGGTG  
GACCAGAAGAAAGGAAAGGTCCCTCTTGCTGTGGCTGCACATCAGGAAGGCTGTGATGGGAATGAA  
GGTGAACAACTGGAGATTTCACTTCAGTCATTGCTTCTGCCTGCAAGATCATCTTTAAAAGTAGAGA  
AGCTGCTCTGTGTGGTGAAGTCAAGAGGAGCAAGTCTGTTCTAGAAGGAAATGGATGCAAGCAGC  
TCCGGGGGGCCCCAAACGCATGCTTCTGTGGTCTAGCCAGGGAAGCCCTTCCGTGGGGGGCCCGCT  
TTGAGGGATGCCACCGGTTCTGGACGCATGGCTGATTCTGAAATGATGATGGTTGCGCCGGGGGCTGCT  
TGCGTGGATTTCCCGGGTGGTGGTTTTGCTGGTGTCTCTCTGCTGTGCTATCTCTGTCTGTACATGT  
TGGCCTGCACCCCAAGGTGACGAGGAGCAGCTGGCACTGCCAGGGCCAACAGCCCCACGGGGAAG  
GAGGGGTACCAGGCCGTCTTTCAGGAGTGGGAGGAGCAGCACCAGCAACTACGTGAGCAGCTGAAGCG  
GCAGATCGCACAGCTCAAGGAGGAGCTGCAGGAGAGGAGTGAGCAGCTCAGGAATGGGCAGTACCAAG  
CCAGCGATGCTGCTGGCCTGGGTCTGGACAGGAGCCCCCAGAGAAAACCCAGGCCGACCTCTGGCC  
TTCTGCACTCGCAGGTGGACAAGGCAGAGGTGAATGCTGGCGTCAAGCTGGCCACAGAGTATGCAGC  
AGTGCTTTTCGATAGCTTTACTCTACAGAAGGTGTACAGCTGGAGACTGGCCTTACCCGCCACCCCG  
AGGAGAAGCCTGTGAGGAAGGACAAGCGGGATGAGTTGGTGAAGCCATTGAATCAGCCTTGGAGACC  
CTGAACAATCCTGCAGAGAACAGCCCCAATCACCGTCTTACACGGCCTCTGATTTTATAGAAGGGAT  
CTACCGAACAGAAAGGGACAAAGGGACATTGTATGAGCTCACCTTCAAAGGGGACCACAAACAGCAAT  
TCAAACGGCTCATCTTATTTTCGACCATTCAGCCCCATCATGAAAGTGAAAAATGAAAGCTCAACATG  
GCCAACACGCTTATCAATGTTATCGTGCTCTAGCAAAAAGGGTGGACAAGTTCCGGCAGTTCATGCA  
GAATTTTCAGGGAGATGTGCATTGAGCAGGATGGGAGAGTCCATCTCACTGTTGTTTACTTTGGGAAAG  
AAGAAATAAATGAAGTCAAAGGAATACTTGAAAACACTTCCAAAGCTGCCAACTTCAGGAACCTTACCT  
TTCATCCAGCTGAATGGAGAATTTTCTCGGGGAAAGGGACTTGATGTTGGAGCCCGCTTCTGGAAGGG  
AAGCAACGTCCTTCTCTTTTCTGTGATGTGGACATCTACTTCACATCTGAATTCCTCAATACGTGTA  
GGCTGAATACACAGCCAGGGAAGAAGGTATTTTATCCAGTCTTTTTCAGTCAGTACAATCCTGGCATA  
ATATACCGCCACCATGATGCAGTCCCTCCCTTGGAACAGCAGCTGGTCATAAAGAAGGAACTGGATT  
TTGGAGAGACTTTGGATTTGGGATGACGTGTGAGTATCGGTGAGCTTCAATATAGGTGGGTTTG  
ATCTGGACATCAAAGGCTGGGGCGGAGAGGATGTGCACCTTTATCGCAAGTATCTCCACAGCAACCTC  
ATAGTGGTACGGACGCTGTGCGAGGACTCTTCCACCTTGGCATGAGAAGCGCTGCATGGACGAGCT  
GACCCCGGAGCAGTACAAGATGTGCATGCAGTCCAAGGCCATGAACGAGGCATCCACGGCCAGCTGG  
GCATGCTGGTGTTCAGGCACGAGATAGAGGCTCACCTTCGCAAAACAGAAACAGAAAGACAAGTAGCAAA  
AAAACATGAAGTCCCAGAGAAGGATTGTGGGAGACACTTTTTCTTTCTTTTGAATTACTGAAAGTG  
GCTGCAACAGAGAAAAGACTTCCATAAAGGACGACAAAAGAAATGGACTGATGGGTGAGAGATGAGAA  
AGCCTCCGATTTCTCTCTGTTGGGCTTTTTTACAACAGAAATCAAATCTCCGCTTTGCTGCAAAAGT  
AACCACAGTTGCACCCCTGTGAAGTGTCTGACAAAGGCAGAATGCTTGTGAGATTATAAGCCTAATGGTG  
TGGAGGTTTTGATGGTGTTTACAATACACTGAGACCTGTTGTTTGTGTGCTCATTGAAATATTCTATG  
ATTTAAGAGCAGTTTTTGTAAAAAATTCATTAGCATGAAAGGCAAGCATATTTCTCTCATATGAATGA  
GCCTATCAGCAGGGCTCTAGTTTCTAGGAATGCTAAAATATCAGAAGGCAGGAGAGGAGATAGGCTTA  
TTATGATACTAGTGAGTACATTAAGTAAATAAAATGGACCAGAAAAGAAAAGAAACCATAAATATCG  
TGTCATATTTTCCCCAAGATTAAACCAAAATAATCTGCTTATCTTTTTGGTTGTCCTTTTAACTGTCT  
CCGTTTTTTTCTTTTATTTAAAAATGCACCTTTTTTCCCTTGTGAGTTATAGTCTGCTTATTTAATTA  
CCACTTTGCAAGCCTTACAAGAGAGCACAAGTTGGCCTACATTTTTATATTTTTTAAGAAGTACTTT  
GAGATGCATTATGAGAACTTTCAAGTCAAGCATCAAATTGATGCCATATCCAAGGACATGCCAAATG  
CTGATTTCTGTGAGGCACTGAATGTGAGGCACTGAGACATAGGGAAGGAATGTTTGTACTAATACAGA  
CGTACAGATACTTTCTCTGAAGAGTATTTTGAAGAGGAGCAACTGAACACTGGAGGAAAAGAAAATG  
ACACTTTCTGCTTTACAGAAAAGGAACTCATTGAGACTGGTGATATCGTGATGTACCTAAAAGTCAG  
AAACCACATTTTCTCTCAGAAGTAGGGACCGCTTTCTTACCTGTTTAAATAAACCAAAAGTATACCGT  
GTGAACCAACAATCTCTTTTCAAAACAGGGTCTCTCTCTGGCTTCTGGCTTCCATAAGAAGAAATG  
GAGAAAAATATATATATATATATATATATTTGTGAAGATCAATCCATCTGCCAGAATCTAGTGGGATG  
GAAGTTTTTGTCTACATGTTATCCACCCAGGCCAGGTGGAAGTAAGTGAATTTTTTAAATTAAGC  
AGTTCTACTCAATCACCAAGATGCTTCTGAAAATGCAATTTATTACCAATTCAAACTATTTTTTAAAT  
AATAAATACAGTTAACATAGAGTGGTTTTCTTCAATCATGTGAAAATTATTAGCCAGCACCAGATGCAT  
GAGCTAATATCTCTTTGAGTCTTTGCTTCTGTTTGTCTCACAGTAACTCATTGTTTAAAGCTTCAA  
GAACATTCAGCTGTTGGTGTGTTAAAAATGCATTGTATTGATTTGTACTGGTAGTTTATGAAATTT  
AATTAACACAGGCCATGAATGGAAGGTGGTATTGCACAGCTAATAAAATATGATTTGTGGATATGAA



FIGURE 276

MMVRRGLLAWISRVVLLVLLCCAISVLYMLACTPKGDEEQALPRANSPTGKEGYQAVLQ  
EWEEQHRNYVSSLKRQIAQLKEELQERSEQLRNGQYQASDAAGLGLDRSPPEKTQADLLAFL  
HSQVDKAEVNAGVKLATEYAAVPFDSFTLQKVYQLETGLTRHPEEKPVKDKRDELVEAIES  
ALETNNPAENSPNHRPYTASDFIEGIYRTERDKGTLYELTFKGDHKHEFKRLILFRPFSP  
MKVKNEKLNMAANTLINVIPLAKRVDKFRQFMQNFREMCIEQDGRVHLTVVYFGKEEINEVK  
GILENTSKAANFRNFTFIQLNGEFSRGKGLDVGARFWKGSNVLLFFCDVDIYFTSEFLNTR  
LNTQPGKKVFYPVLF SQYNPGIIYGHDAVPPLEQQLVIKKETGFWRDFGFGMTQYRSDFI  
NIGGFDDIKGWGGEDVHLYRKYLHSNLIVV RTPVRGLFHLWHEKRCMDLTPEQYKMCMQS  
KAMNEASHGQLGMLVFRHEIEAHLRKQKQKTSSKKT

FIGURE 277

GAAAGAATGTTGTGGCTGCTCTTTTTCTGGTGA CTGCCATTCATGCTGAACTCTGTCAACC  
AGGTGCAGAAAATGCTTTTAAAGTGAGACTTAGTATCAGAACAGCTCTGGGAGATAAAGCAT  
ATGCCTGGGATACCAATGAAGAATACCTCTTCAAAGCGATGGTAGCTTTCTCCATGAGAAAA  
GTTCCCAACAGAGAAGCAACAGAAATTTCCCATGTCCTACTTTGCAATGTAACCCAGAGGGT  
ATCATTCTGGTTTGTGGTTACAGACCCCTTCAAAAAATCACACCCTTCCTGCTGTTGAGGTGC  
AATCAGCCATAAGAATGAACAAGAACCGGATCAACAATGCCTTCTTTCTAAATGACCAACT  
CTGGAATTTTTTAAAAATCCCTTCCACACTTGCACCACCCATGGACCCATCTGTGCCCATCTG  
GATTATTATATTTGGTGTGATATTTTGCATCATCATAGTTGCAATTGCCTACTGATTTTTAT  
CAGGGATCTGGCAACGTAGAAGAAAGAACAAAGAACCATCTGAAGTGGATGACGCTGAAGAT  
AAGTGTGAAAACATGATCACAATTGAAATGGCATCCCTCTGATCCCCTGGACATGAAGGG  
GGGCATATTAATGATGCCTTCATGACAGAGGATGAGAGGCTCACCCTCTCTGAAGGGCTGT  
TGTTCTGCTTCCTCAAGAAATTAAACATTTGTTTCTGTGTGACTGCTGAGCATCCTGAAATA  
CCAAGAGCAGATCATATATTTTGTTCACCATTCTTCTTTTGTAATAAATTTTGAATGTGCT  
TGAAAGTGAAAAGCAATCAATTATACCCACCAACACCACTGAAATCATAAGCTATTCACGAC  
TCAAAATATTCTAAAATATTTTTCTGACAGTATAGTGTATAAATGTGGTCATGTGGTATTTG  
TAGTTATTGATTTAAGCATTTTGTAGAAATAAGATCAGGCATATGTATATATTTTACACTTC  
AAAGACCTAAGGAAAAATAAATTTTCCAGTGGAGAATACATATAATATGGTGTAGAAATCAT  
TGAAAATGGATCCTTTTTTGACGATCACTTATATCACTCTGTATATGACTAAGTAAACAAAAG  
TGAGAAGTAATTATTGTAAATGGATGGATAAAAAATGGAATTACTCATATACAGGGTGGAATT  
TTATCCTGTTATCACACCAACAGTTGATTATATATTTTCTGAATATCAGCCCCTAATAGGAC  
AATTCTATTTGTTGACCATTTCTACAATTTGTAAAAGTCCAATCTGTGCTAACTTAATAAAG  
TAATAATCATCTCTTTTTTAAAAAAAAAAAAAAAAAAAAAAAAAAAAA

FIGURE 278

MLWLLFFLVTAIHAELCQPGAENAFKVRLSIRTALGDKAYAWDTNEEYLFKAMVAFSMRKVP  
NREATEISHVLLCNVTQRVSFVFWVTDPSKNHTLPAVEVQSAIRMNKNRINNAFFLNDQTLE  
FLKIPSTLAPPMDPSVPIWIIIFGVIFCIIIVAIALLILSGIWQRRRKNKEPSEVDDAEDKC  
ENMITIENGIPSDPLDMKGGILMMPS

FIGURE 279

AACTCAAACCTCTCTCTCTGGGAAAACGCGGTGCTTGCTCCTCCCGGAGTGGCCTTGGCAGG  
GTGTTGGAGCCCTCGGTCTGCCCCGTCCGGTCTCTGGGGCCAAGGCTGGGTTTCCCTCATGT  
ATGGCAAGAGCTCTACTCGTGCGGTGCTTCTTCTCCTTGGCATAACAGCTCACAGCTCTTTGG  
CCTATAGCAGCTGTGGAAATTTATACCTCCCGGGTGCTGGAGGCTGTTAATGGGACAGATGC  
TCGGTTAAAATGCACTTTCTCCAGCTTTGCCCCGTGGGTGATGCTCTAACAGTGACCTGGA  
ATTTTCGTCCTCTAGACGGGGGACCTGAGCAGTTTGTATTCTACTACCACATAGATCCCTTC  
CAACCCATGAGTGGGCGGTTTAAGGACCGGTGTCTTGGGATGGGAATCCTGAGCGGTACGA  
TGCCTCCATCCTTCTCTGGAAACTGCAGTTCGACGACAATGGGACATACACCTGCCAGGTGA  
AGAACCCACCTGATGTTGATGGGGTGATAGGGGAGATCCGGCTCAGCGTCGTGCACACTGTA  
CGCTTCTCTGAGATCCACTTCCTGGCTCTGGCCATTGGCTCTGCCTGTGCACTGATGATCAT  
AATAGTAATTGTAGTGGTCCTCTTCCAGCATTACCGGAAAAAGCGATGGGCCGAAAGAGCTC  
ATAAAGTGGTGGAGATAAAATCAAAGAAGAGGAAAGGCTCAACCAAGAGAAAAAGGTCTCT  
GTTTATTTAGAAGACACAGACTAAACAATTTTAGATGGAAGCTGAGATGATTTCCAAGAACAA  
GAACCCTAGTATTTCTTGAAGTTAATGGAACTTTTCTTTGGCTTTTCCAGTTGTGACCCGT  
TTTCCAACCAGTTCTGCAGCATATTAGATTCTAGACAAGCAACACCCCTCTGGAGCCAGCAC  
AGTGCTCCTCCATATCACCAGTCATACACAGCCTCATTATTAAGGTCTTATTTAATTTCAGA  
GTGTAAATTTTTTCAAGTGCTCATTAGGTTTTATAAACAAGAAGCTACATTTTTGCCCTTAA  
GACACTACTTACAGTGTTATGACTTGTATACACATATATTGGTATCAAAGGGGATAAAAGCC  
AATTTGTCTGTTACATTTCTTTTACGTATTTCTTTTAGCAGCACTTCTGCTACTAAAGTTA  
ATGTGTTTACTCTCTTCTTCCACATTCTCAATTAAAAGGTGAGCTAAGCCTCCTCGGTG  
TTTCTGATTAACAGTAAATCCTAAATTCAAACGTGTTAAATGACATTTTTATTTTTATGTCTC  
TCCTTAACTATGAGACACATCTTGTTTTACTGAATTTCTTTCAATATTCCAGGTGATAGATT  
TTTGTCG

FIGURE 280

MYGKSSTRAVLLLLLGIQLTALWPAAVEIYTSRVLEAVNGTDARLKCTFSSFAPVGDALTVT  
WNFRPLDGGPEQFVFYYHIDPFQPMSGFRFKDRVSWDGNPERYDASILLWKLQFDDNGTYTCQ  
VKNPPDVDGVIGEIRLSVVHTVRFSEIHFLALAIGSACALMIIIVIVVVLFQHYRKKRWAER  
AHKVVEIKSKEEERLNQEKKVSVYLEDTD

FIGURE 281

GCATTTTTGTCTGTGCTCCCTGATCTTCAGGTCACCACCATGAAGTTCTTAGCAGTCCTGGT  
ACTCTTGGGAGTTTCCATCTTTCTGGTCTCTGCCCAGAATCCGACAACAGCTGCTCCAGCTG  
ACACGTATCCAGCTACTGGTCCTGCTGATGATGAAGCCCCTGATGCTGAAACCACTGCTGCT  
GCAACCACTGCGACCACTGCTGCTCCTACCACTGCAACCACCGCTGCTTCTACCACTGCTCG  
TAAAGACATTCCAGTTTTACCCAAATGGGTTGGGGATCTCCCGAATGGTAGAGTGTGTCCCT  
GAGATGGAATCAGCTTGAGTCTTCTGCAATTGGTCACAACTATTCATGCTTCCTGTGATTTC  
ATCCAACCTACTTACCTTGCCTACGATATCCCCTTTATCTCTAATCAGTTTATTTCTTTCAA  
ATAAAAAATAACTATGAGCAACATAAAAAAAAAAAAAA

FIGURE 282

MKFLAVLVLLGVSIFLVSAQNPTTAAPADTYPATGPADDEAPDAETTAAATTATTAAPTAT  
TAASTTARKDIPVLPKWVDLPNGRVCP

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FIGURE 283

GGACTCTGAAGGTCCCAAGCAGCTGCTGAGGCCCCCAAGGAAGTGGTTCCAACCTTGGACCC  
CTAGGGGTCTGGATTTGCTGGTTAACAAGATAACCTGAGGGCAGGACCCCATAGGGGAATGC  
TACCTCCTGCCCTTCCACCTGCCCTGGTGTTCACGGTGGCCTGGTCCCTCCTTGCCGAGAGA  
GTGTCCTGGGTGAGGACGAGAGGACGCTCACAGACTCCAGCCCTTTGTTACCGAGAGGAC  
ACTTGGCAAGGTCCAGCGATGGTCCGGAGTCCACACACAGACTGGCGGCAGGGCAGGAGGGG  
GACAGTTCCTGTTGTGCTTGGTTGGACAGTAAGAGGGTCTTGGCCAGTCCAGGGTGGGGGGCG  
GCAAACCTCCATAAAGAACCAGAGGGTCTGGGCCCCGGCCACAGAGTCATCTGCCAGCTCCT  
CTGCTGCTGGCCAGTGGGAGTGGCACGAGGTGGGGCTTTGTGCCAGTAAACCACAGGCTGG  
ATTTGCCTGCGGGCCATGGTCCCTGTCTAGGGCAGCAATTCTCAACCTTCTTGCTCTCAGGA  
CCCCAAAGAGCTTTCATTGTATCTATTGATTTTTTACCACATTAGCAATTAAAACTGAGAAAT  
GGGCCGGGCACGGTGGCTCACGCCTGTAATCCCAGCACTTTGGGAGGCCGAGGCGGGTGGAT  
CACCTGAGATCAGGAGTTCAAGACCAGCCTGGCCAACATGGTGAAACCTTGTCTACTAAAAA  
TACAAAAAATTAGCCAGGCACAGTGGTGTGCACTGGTAGTCCCAGTTACTCGGGAGGCTGAG  
GCAGGAAAATCGCTTGAACCCAGGAGGCGGACGTTGCGGTGAGCCGAGATCGCGCCGCTGAT  
TCCAGCCTGGGCGACAAGAGTGAGACTCCATCTCACACA



FIGURE 284

MLPPALPPALVFTVAWSLLAERVSWVRDAEDAHRLQPFVTERTLGKVQRWSGVHTQTGGRAG  
GGQFCCAWLDSKRVLASPGWGAANSIKNQRVWAPATESSAQLCCWPVGVARGGALCQ

FIGURE 285

GTCATGCCAGTGCCTGCTCTGTGCCTGCTCTGGGCCCTGGCAATGGTGACCCGGCCTGCCTCA  
GCGGCCCCCATGGGCGGCCCAGAACTGGCACAGCATGAGGAGCTGACCCTGCTCTTCCATGG  
GACCCTGCAGCTGGGCCAGGCCCTCAACGGTGTGTACAGGACCACGGAGGGACGGCTGACAA  
AGGCCAGGAACAGCCTGGGTCTCTATGGCCGCACAATAGAACTCCTGGGGCAGGAGGTGAGC  
CGGGGCCGGGATGCAGCCAGGAACTTCGGGCAAGCCTGTTGGAGACTCAGATGGAGGAGGA  
TATTCTGCAGCTGCAGGCAGAGGCCACAGCTGAGGTGCTGGGGGAGGTGGCCCAGGCACAGA  
AGGTGCTACGGGACAGCGTGCAGCGGCTAGAAGTCCAGCTGAGGAGCGCCTGGCTGGGCCCT  
GCCTACCGAGAAATTTGAGGTCTTAAAGGCTCACGCTGACAAGCAGAGCCACATCCTATGGGC  
CCTCACAGGCCACGTGCAGCGGCAGAGGCGGGAGATGGTGGCACAGCAGCATCGGCTGCGAC  
AGATCCAGGAGAGACTCCACACAGCGGCGCTCCCAGCCTGAATCTGCCTGGATGGAACTGAG  
GACCAATCATGCTGCAAGGAACACTTCCACGCCCCGTGAGGCCCTGTGCAGGGAGGAGCTG  
CCTGTTCACTGGGATCAGCCAGGGCGCCGGGCCCCACTTCTGAGCACAGAGCAGAGACAGAC  
GCAGGCGGGGACAAAGGCAGAGGATGTAGCCCCATTGGGGAGGGGTGGAGGAAGGACATGTA  
CCCTTTCATGCCTACACCCCCCTATTAAAGCAGAGTCGTGGCATTTCAAAAAAAAAAAAAA  
AAAAAAAAAAAAAAAAAAAAAAAAAAAA

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FIGURE 286

MPVPALCLLWALAMVTRPASAAPMGGPELAQHEELTLLFHGTLQLGQALNGVYRTTEGRLTK  
ARNSLGLYGRTIELLGQEVSRGRDAAQELRASLLETQMEEDILQLQAEATAEVLGEVAQAQK  
VLRDSVQRLEVQLRSAWLGPAYREFEVLKAHADKQSHILWALTGHVQRQRREMVAAQQHRLRQ  
IQERLHTAALPA

FIGURE 287

GGCAACATGGCTCAGCAGGCTTGCCCCAGAGCCATGGCAAAGAATGGACTTGTAATTTGCAT  
CCTGGTGATCACCTTACTCTGGACCAGACCACCAGCCACACATCCAGATTAAAAGCCAGGA  
AGCACAGCAAACGTCGAGTGAGAGACAAGGATGGAGATCTGAAGACTCAAATTGAAAAGCTC  
TGGACAGAAGTCAATGCCTTGAAGGAAATTCAAGCCCTGCAGACAGTCTGTCTCCGAGGCAC  
TAAAGTTCACAAGAAATGCTACCTTGCTTCAGAAGGTTTGAAGCATTTCATGAGGCCAATG  
AAGACTGCATTTCCAAAGGAGGAATCCTGGTTATCCCCAGGAACTCCGACGAAATCAACGCC  
CTCCAAGACTATGGTAAAAGGAGCCTGCCAGGTGTCAATGACTTTTGGCTGGGCATCAATGA  
CATGGTCACGGAAGGCAAGTTTGTGACGTCAACGGAATCGCTATCTCCTTCTCAACTGGG  
ACCGTGACAGCCTAACGGTGGCAAGCGAGAAAACTGTGTCTGTCTCCCAATCAGCTCAG  
GGCAAGTGGAGTGATGAGGCCTGTGCGCAGCAGCAAGAGATACATATGCGAGTTCACCATCCC  
TAAATAGGTCTTTCTCCAATGTGTCTCCAAGCAAGATTCATCATAACTTATAGGTTTCATGA  
TCTCTAAGATCAAGTAAAAATCATAATTTTTACTTTATTAATAAATTGCAACACAAGATCAAT  
GTCCATAGCAATATGATAGCATCAGCCAATTTTGCTAACACATTTCTTTGGGATTTTGCCCT  
TCCTGGGGTATAGGGGATCAGAAATATTGATCCATGTGCACGCAGATAAAATGGCTTCTGCT  
AAACAGACTAAAATCTTTCTCTTAGTCTTTCTCACTTGTACAAACCCAGTTTGTTTTCAA  
AAATCACAGTAGCAATGCAACTCATCACTCTAGAAAAGCAAGCTTAGGCTACCTGAAAGATT  
TTCCCTTGGAAGTTTAGCGTATGTTTGACTAACAAAAATCCCTACATCAGAGACTCTAGGT  
GCTATATAATCCAAAACTTTTCAGCCTGTGCTCATTCTGTCCCATGCTGGCAATAATACC  
TTGTGAGCCCATTAACCTTATTTTGAATTGCTCCATCTCCTGGTGGGACTTGTATCTTGTCT  
GCCATATCAGAACACAAACCCCTGAAGAGGTTCTGATTTGATTTTTTTTTTTTCTTCATGCC  
TACCCTTTTTTTTGGAAGTTTCCAGCCGCAATTTGAAATGAAATGACAAGGTGTATATTGAT  
CAATTTTCATTCCCACCATTCGATTACAACCTCTAACTTAAATGGGTAAACCTAAGGCATAT  
CAAAGAAGCAGATTGCATGATAAACGGAAATAGAAAAAAGAACCTACATTTATTTTGCTTT  
AGCATCCTTACTCTCACCTTTTATGAGATTGAGAGTGGACTTACATTTCTTTTTTACATTT  
TCGTATATTTATTTTTTTTAGCCATCATTATATGTTTAAGTCTATTATGGGCAACCAATCTT  
TGGAAGCTGAAAACCTGAATTTAAAGAATGCTATCTTGAAAAATTGCATACGTCTGTGCAATT  
TTTTATTCTGCCTAGTGCTATTCTGCTTGTTTAACTAGATTGTACAAAATAACTTCATTGCT  
TAATATCAAATTACAAAGTTTAGACTTGGAGGAAATGGGCTTTTAGAAGCAAACAATTTT  
AAATATATTTTGTCTTCAAATAAATAGTGTTTAAACATTGAATGTGTTTTGTGAACAATAT  
CCCCTTTGCAAACCTTAACTACACATGCTTGGAATTAAGTTTTAGCTGTTTTTCATTGCTCA  
ATAATAAAGCCTGAATTCTGATCAATAAAAAAAAAAAAAAAAAAAAAAAAAAAAAA

FIGURE 288

MAQQACPRAMAKNGLVICILVITLLLDQTTSHTSRLKARKHSKRRVRDKDGLKTQIEKLWT  
EVNALKEIQALQTVCLRGTKVHKKCYLASEGLKHFHEANEDCISKGGILVIPRNSDEINALQ  
DYGKRSLPGVNDFWLGINDMVTEGKFVDVNGIAISFLNWDRAQPNGGKRENCVLFSQSAQ GK  
WSDEACRSSKRYICEFTIPK

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FIGURE 289

GCGAGGACCGGGTATAAGAAGCCTCGTGGCCTTGCCCGGGCAGCCGCAGGTTCCCCGCGCGC  
CCCCAGCCCCCGCGCCATGAAGCTCGCCGCCCTCCTGGGGCTCTGCGTGGCCCTGTCCTGCA  
GCTCCGCTGCTGCTTTCTTAGTGGGCTCGGCCAAGCCTGTGGCCCAGCCTGTGCTGCGCTG  
GAGTCGGCGGCGGAGGCCGGGGCCGGGACCCTGGCCAACCCCCCTCGGCACCCCTCAACCCGCT  
GAAGCTCCTGCTGAGCAGCCTGGGCATCCCCGTGAACACCTCATAGAGGGCTCCCAGAACT  
GTGTGGCTGAGCTGGGTCCCCAGGCCGTGGGGGCCGTGAAGGCCCTGAAGGCCCTGCTGGGG  
GCCCTGACAGTGTTTGGCTGAGCCGAGACTGGAGCATCTACACCTGAGGACAAGACGCTGCC  
CACCCGCGAGGGCTGAAAACCCCGCCGCGGGGAGGACCGTCCATCCCCTTCCCCCGGCCCT  
CTCAATAAACGTGGTTAAGAGCAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAA  
AAAAAAAAAAAA

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FIGURE 290

MKLAALLGLCVALSCSSAAAFVGSAPVAPVAALESAAEAGAGTLANPLGTLNPLKLLLS

SLGIPVNHLEGSQKCVNELGPQAVGAVKALKALLGALTVFG

FIGURE 291

TGAAGGACTTTTCCAGGACCCAAGGCCACACACTGGAAGTCTTGCAGCTGAAGGGAGGCACT  
CCTTGGCCTCCGCAGCCGATCACATGAAGGTGGTGCCAAGTCTCCTGCTCTCCGTCCTCCTG  
GCACAGGTGTGGCTGGTACCCGGCTTGGCCCCAGTCTCAGTCGCCAGAGACCCCAGCCCC  
TCAGAACCAGACCAGCAGGGTAGTGCAGGCTCCCAGGGAGGAAGAGGAAGATGAGCAGGAGG  
CCAGCGAGGAGAAGGCCGGTGAGGAAGAGAAAGCCTGGCTGATGGCCAGCAGGCAGCAGCTT  
GCCAAGGAGACTTCAAACCTTCGGATTTCAGCCTGCTGCGAAAGATCTCCATGAGGCACGATGG  
CAACATGGTCTTCTCTCCATTTGGCATGTCTTGGCCATGACAGGCTTGATGCTGGGGGCCA  
CAGGGCCGACTGAAACCCAGATCAAGAGAGGGGCTCCACTTGCAGGCCCTGAAGCCCACCAAG  
CCCGGGCTCCTGCCTTCCCTCTTTAAGGGACTCAGAGAGACCCCTCTCCCGCAACCTGGAAC  
GGGCCTCTCACAGGGGAGTTTTGCCTTCATCCACAAGGATTTTGATGTCAAAGAGACTTTCT  
TCAATTTATCCAAGAGGTATTTTGATACAGAGTGCCTGCCTATGAATTTTCGCAATGCCTCA  
CAGGCCAAAAGGCTCATGAATCATTACATTAAACAAAGAGACTCGGGGAAAATTCCCAAAC  
GTTTGATGAGATTAATCCTGAAACCAAATTAATTCTTGTGGATTACATCTTGTTCAAAGGGA  
AATGGTTGACCCCATTTGACCCTGTCTTCACCGAAGTCGACACTTTCACCTGGACAAGTAC  
AAGACCATTAAGGTGCCCATGATGTACGGTGCAGGCAAGTTTGCCTCCACCTTTGACAAGAA  
TTTTCGTTGTATGTCTCAAACCTGCCCTACCAAGGAAATGCCACCATGCTGGTGGTCTCA  
TGGAGAAAATGGGTGACCACCTCGCCCTGAAGACTACCTGACCACAGACTTGGTGGAGACA  
TGGCTCAGAAAACATGAAAACAGAAACATGGAAGTTTCTTCCGAAGTTCAAGCTAGATCA  
GAAGTATGAGATGCATGAGCTGCTTAGGCAGATGGGAATCAGAAGAATCTTCTCACCCCTTG  
CTGACCTTAGTGAACTCTCAGCTACTGGAAGAAATCTCCAAGTATCCAGGGTTTTACGAAGA  
ACAGTGATTGAAGTTGATGAAAGGGGCACTGAGGCAGTGGCAGGAATCTTGTGAGAAATTAC  
TGCTTATTCATGCCTCCTGTATCAAAGTGGACCGGCCATTTCAATTCATGATCTATGAAG  
AAACCTCTGGAATGCTTCTGTTTCTGGGCAGGGTGGTGAATCCGACTCTCCTATAATTCAGG  
ACATGCATAAGCACTTCGTGCTGTAGTAGATGCTGAATCTGAGGTATCAAACACACACAGGA  
TACCAGCAATGGATGGCAGGGGAGAGTGTTCTTTTGTCTTAACTAGTTAGGGTGTCTC  
AAATAAATACAGTAGTCCCCACTTATCTGAGGGGGATACATTCAAAGACCCCCAGCAGATGC  
CTGAAACGGTGGACAGTGCTGAACCTTATATATATTTTTTCTACACATACATACCTATGAT  
AAAGTTTAAATTTATAAATTAGGCACAGTAAGAGATTAACAATAATAACAACATTAAGTAAAA  
TGAGTTACTTGAAACGCAAGCACTGCAATACCATAACAGTCAAACCTGATTATAGAGAAGGCTA  
CTAAGTGACTCATGGGCGAGGAGCATAGACAGTGTGGAGACATTGGGCAAGGGGAGAAATCA  
CATCCTGGGTGGGACAGAGCAGGACGATGCAAGATTCATCCCACTACTCAGAATGGCATGC  
TGCTTAAGACTTTTAGATTGTTTATTTCTGGAATTTTCATTTAATGTTTTTGGACCATGGT  
TGACCATGGTTAACTGAGACTGCAGAAAGCAAAACCATGGATAAGGGAGGACTACTACAAAA  
GCATTAAATTGATACATATTTTTTAAAAA



FIGURE 292

MKVVP S L L L S V L L A Q V W L V P G L A P S P Q S P E T P A P Q N Q T S R V V Q A P R E E E E D E Q E A S E E K A G E  
E E K A W L M A S R Q Q L A K E T S N F G F S L L R K I S M R H D G N M V F S P F G M S L A M T G L M L G A T G P T E T Q I  
K R G L H L Q A L K P T K P G L L P S L F K G L R E T L S R N L E L G L S Q G S F A F I H K D F D V K E T F F N L S K R Y F  
D T E C V P M N F R N A S Q A K R L M N H Y I N K E T R G K I P K L F D E I N P E T K L I L V D Y I L F K G K W L T P F D P  
V F T E V D T F H L D K Y K T I K V P M M Y G A G K F A S T F D K N F R C H V L K L P Y Q G N A T M L V V L M E K M G D H L  
A L E D Y L T T D L V E T W L R N M K T R N M E V F F P K F K L D Q K Y E M H E L L R Q M G I R R I F S P F A D L S E L S A  
T G R N L Q V S R V L R R T V I E V D E R G T E A V A G I L S E I T A Y S M P P V I K V D R P F H F M I Y E E T S G M L L F  
L G R V V N P T L L

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FIGURE 293

CTGGGATCAGCCACTGCAGCTCCCTGAGCACTCTCTACAGAGACGCGGACCCCAGACATGAG  
GAGGCTCCTCCTGGTCACCAGCCTGGTGGTTGTGCTGCTGTGGGAGGCAGGTGCAGTCCCAG  
CACCCAAGGTCCCTATCAAGATGCAAGTCAAACACTGGCCCTCAGAGCAGGACCCAGAGAAG  
GCCTGGGGCGCCCGTGTGGTGGAGCCTCCGGAGAAGGACGACCAGCTGGTGGTGTCTGTTCCC  
TGTCAGAAAGCCGAAACTCTTGACCACCGAGGAGAAGCCACGAGGTCAGGGCAGGGGCCCCA  
TCCTTCCAGGCACCAAGGCCTGGATGGAGACCGAGGACACCCTGGGCCGTGTCCTGAGTCCC  
GAGCCCGACCATGACAGCCTGTACCACCCTCCGCCTGAGGAGGACCAGGGCGAGGAGAGGCC  
CCGGTTGTGGGTGATGCCAAATCACCAGGTGCTCCTGGGACCGGAGGAAGACCAAGACCACA  
TCTACCACCCCCAGTAGGGCTCCAGGGGCCATCACTGCCCCCGCCCTGTCCCAAGGGCCAGG  
CTGTTGGGACTGGGACCCTCCCTACCCTGCCCCAGCTAGACAAATAAACCCAGCAGGCAAA  
AAAAAAAAAAAAAAAA

FIGURE 294

MRLLLLVTSLVVLLWEAGAVPAPKVPIKMQVKHWPSEQDPEKAWGARVVEPPEKDDQLVVL  
FPVQKPKLLTTEEKPRGQGRGPILPGTKAWMETEDTLGRVLSPEPDHDSLYHPPPEEDQGEE  
RRLWVMPNHQVLLGPEEDQDHIYHPQ

FIGURE 295

AGAAAGCTGCACTCTGTTGAGCTCCAGGGCCGAGTGGAGGGAGGGAGTGAAGGAGCTCTCTG  
TACCCAAGGAAAGTGCAGCTGAGACTCAGACAAGATTACAATGAACCAACTCAGCTTCCTGC  
TGTTTCTCATAGCGACCACCAGAGGATGGAGTACAGATGAGGCTAATACTTACTTCAAGGAA  
TGGACCTGTTCTTCGTCTCCATCTCTGCCCAGAAAGCTGCAAGGAAATCAAAGACGAATGTCC  
TAGTGCAATTTGATGGCCTGTATTTTCTCCGCACTGAGAATGGTGTATCTACCAGACCTTCT  
GTGACATGACCTCTGGGGGTGGCGGCTGGACCCTGGTGGCCAGCGTGCAATGAGAATGACATG  
CGTGGGAAGTGCACGGTGGGCGATCGCTGGTCCAGTCAGCAGGGCAGCAAAGCAGACTACCC  
AGAGGGGGACGGCAACTGGGCCAACTACAACACCTTTGGATCTGCAGAGGCGGCCACGAGCG  
ATGACTACAAGAACCCTGGCTACTACGACATCCAGGCCAAGGACCTGGGCATCTGGCACGTG  
CCCAATAAGTCCCCCATGCAGCACTGGAGAAACAGCTCCCTGCTGAGGTACCGCACGGACAC  
TGGCTTCCTCCAGACACTGGGACATAATCTGTTTGGCATCTACCAGAAATATCCAGTGAAAT  
ATGGAGAAGGAAAGTGTGGACTGACAACGGCCCGGTGATCCCTGTGGTCTATGATTTTGGC  
GACGCCCAGAAAACAGCATCTTATTACTCACCTATGGCCAGCGGGAATTCAGTGCGGGATT  
TGTTCAAGTTCAGGGTATTTAATAACGAGAGAGCAGCCAACGCCTTGTGTGCTGGAATGAGGG  
TCACCGGATGTAACACTGAGCATCACTGCATTGGTGGAGGAGGATACTTTCCAGAGGCCAGT  
CCCCAGCAGTGTGGAGATTTTCTGGTTTTGATTGGAGTGGATATGGAACTCATGTTGGTTA  
CAGCAGCAGCCGTGAGATAACTGAGGCAGCTGTGCTTCTATTCTATCGTTGAGAGTTTTGTG  
GGAGGGAACCCAGACCTCTCCTCCCAACCATGAGATCCCAAGGATGGAGAACAACCTTACCCA  
GTAGCTAGAATGTTAATGGCAGAAGAGAAAACAATAAATCATATTGACTCAAGAAAAAAA

FIGURE 296

MNQLSFLLFLIATTRGWSTDEANTYFKEWTCSSSPSLPRSCKEIKDECPSAFDGLYFLRTEN  
GVIYQTFCDMTSGGGGWTLVASVHENDMRGKCTVGDRWSSQQGSKADYPEGDGNWANYNTFG  
SAEAATSDDYKNPGYYDIQAKDLGIWHVPNKSPMQHWRNSSLLRYRTDTGFLQTLGHNLFGI  
YQKYPVKYGEKGCWTDNGPVI PVVYDFGDAQKTASYSPYGQREFTAGFVQFRVFNNERAAN  
ALCAGMRVTGCNTEHHCIGGGGYFPEASPPQCGDFSGFDWSGYGTHVGYSSSREITEAAVLLFYR

FIGURE 297

GCGGAGCCGGCGCCGGCTGCGCAGAGGAGCCGCTCTCGCCGCCGCCACCTCGGCTGGGAGCC  
CACGAGGCTGCCGCATCCTGCCCTCGGAACAATGGGACTCGGCGCGCGAGGTGCTTGGGCCG  
CGCTGCTCCTGGGGACGCTGCAGGTGCTAGCGCTGCTGGGGGCCGCCCATGAAAGCGCAGCC  
ATGGCGGCATCTGCAAAACATAGAGAATTCTGGGCTTCCACACAACCTCCAGTGCTAACTCAAC  
AGAGACTCTCCAACATGTGCCTTCTGACCATACAAATGAAACTTCCAACAGTACTGTGAAAC  
CACCAACTTCAGTTGCCCTCAGACTCCAGTAATACAACGGTCACCACCATGAAACCTACAGCG  
GCATCTAATACAACAACACCAGGGATGGTCTCAACAAATATGACTTCTACCACCTTAAAGTC  
TACACCCAAAACAACAAGTGTTTCACAGAACACATCTCAGATATCAACATCCACAATGACCG  
TAACCCACAATAGTTCAGTGACATCTGCTGCTTCATCAGTAACAATCACAACAACCTATGCAT  
TCTGAAGCAAAGAAAGGATCAAATTTGATACTGGGAGCTTTGTTGGTGGTATTGTATTAAAC  
GCTGGGAGTTTTATCTATTCTTTACATTGGATGCAAAATGTATTACTCAAGAAGAGGCATTC  
GGTATCGAACCATAGATGAACATGATGCCATCATTTAAGGAAATCCATGGACCAAGGATGGA  
ATACAGATTGATGCTGCCCTATCAATTAAATTTGGTTTTATTAATAGTTTAAAAACAATATTCT  
CTTTTTGAAAATAGTATAAACAGGCCATGCATATAATGTACAGTGTATTACGTAAATATGTA  
AAGATTCTTCAAGGTAACAAGGGTTTGGGTTTTGAAATAAACATCTGGATCTTATAGACCGT  
TCATACAATGGTTTTAGCAAGTTCATAGTAAGACAAACAAGTCCTATCTTTTTTTTTTGGCT  
GGGGTGGGGGCATTGGTCACATATGACCAGTAATTGAAAGACGTCATCACTGAAAGACAGAA  
TGCCATCTGGGCATACAAATAAGAAGTTTGTACAGCACTCAGGATTTTGGGTATCTTTTGT  
AGCTCACATAAAGAACTTCAGTGCTTTTCAGAGCTGGATATATCTTAATTACTAATGCCACA  
CAGAAATTATACAATCAAACCTAGATCTGAAGCATAATTTAAGAAAAACATCAACATTTTTTG  
TGCTTTAACTGTAGTAGTTGGTCTAGAAACAAAATACTCC

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FIGURE 298

MGLGARGAWAALLLGTLQVLALLGAAHESAAMAASANIENSGLPNSSANSTETLQHVP  
SDH  
TNETSNSTVKPPTSVASDSSNTTVTTMKPTAASNTTTPGMVSTNMTSTTLKSTPKTTSVSQ  
N  
TSQISTSTMVTHNSSVTSAASSVTITTTMHSEAKKGSKFDTGSFVGGIVLTLGVLSILYIG  
CKMYYSRRGIRYRTIDEHDAII

FIGURE 299

CAGCCGGGTCCCAAGCCTGTGCCTGAGCCTGAGCCTGAGCCTGAGCCCGAGCCGGGAGCCGG  
TCGCGGGGGCTCCGGGCTGTGGGACCGCTGGGCCCCAGCGATGGCGACCCTGTGGGGAGGC  
CTTCTTCGGCTTGGCTCCTTGCTCAGCCTGTGCTGCCTGGCGCTTCCGTGCTGCTGCTGGC  
GCAGCTGTCAGACGCCGCCAAGAATTCGAGGATGTCAGATGTAAATGTATCTGCCCTCCCT  
ATAAAGAAAATTCTGGGCATATTTATAATAAGAACATATCTCAGAAAGATTGTGATTGCCTT  
CATGTTGTGGAGCCCATGCCTGTGCGGGGGCCTGATGTAGAAGCATACTGTCTACGCTGTGA  
ATGCAAATATGAAGAAAGAAGCTCTGTCACAATCAAGGTTACCATTATAATTTATCTCTCCA  
TTTTGGGCCTTCTACTTCTGTACATGGTATATCTTACTCTGGTTGAGCCCATACTGAAGAGG  
CGCCTCTTTGGACATGCACAGTTGATACAGAGTGATGATGATATTGGGGATCACCAGCCTTT  
TGCAAATGCACACGATGTGCTAGCCCGCTCCCGCAGTCGAGCCAACGTGCTGAACAAGGTAG  
AATATGCACAGCAGCGCTGGAAGCTTCAAGTCCAAGAGCAGCGAAAGTCTGTCTTTGACCGG  
CATGTTGTCTCAGCTAATTGGGAATTGAATTCAAGGTGACTAGAAAGAAACAGGCAGACAA  
CTGGAAGAAGTACTGGGTTTTGCTGGGTTTCATTTTAATACCTTGTTGATTTTACCAACT  
GTTGCTGGAAGATTCAAAAGTGAAGCAAAAAGTCTTGCTTGATTTTTTTTTCTTGTTAACGTA  
ATAATAGAGACATTTTTTAAAGCACACAGCTCAAAGTCAGCCAATAAGTCTTTTCTATTTG  
TGACTTTTACTAATAAAAATAAATCTGCCTGTAAATTATCTTGAAGTCCTTTACCTGGAACA  
AGCACTCTCTTTTTTACCACATAGTTTTAACTTGACTTTCAAGATAATTTTACGGGTTTTTG  
TTGTTGTTGTTTTTTGTTTGTGTTTTGGTGGGAGAGGGGAGGGATGCCTGGGAAGTGGTT  
AACAACTTTTTTCAAGTCACTTTACTAAACAACTTTTGTAATAGACCTTACCTTCTATTT  
TCGAGTTTCATTTATATTTTGCAGTGTAGCCAGCCTCATCAAAGAGCTGACTTACTCATTTG  
ACTTTTGCACTGACTGTATTATCTGGGTATCTGCTGTGTCTGCACTTCATGGTAAACGGGAT  
CTAAAATGCCTGGTGGCTTTTCAAAAAAGCAGATTTTCTTCATGTACTGTGATGTCTGATG  
CAATGCATCCTAGAACAACTGGCCATTTGCTAGTTTACTCTAAAGACTAAACATAGTCTTG  
GTGTGTGTGGTCTTACTCATCTTCTAGTACCTTTAAGGACAAATCCTAAGGACTTGGACACT  
TGCAATAAAGAAATTTTATTTTAAACCAAGCCTCCCTGGATTGATAATATATACACATTTG  
TCAGCATTTCCGGTCGTGGTGAGAGGCAGCTGTTTGAGCTCCAATATGTGCAGCTTTGAACT  
AGGGCTGGGGTTGTGGGTGCCTCTTCTGAAAGGTCTAACCATTATTGGATAACTGGCTTTTT  
TCTTCTATGTCCTCTTTGGAATGTAAACAATAAAAATAATTTTTGAAACATCAA



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FIGURE 300

MATLWGGLRLGSLLSLSCLALSVLLLAQLSDAAKNFEDVRCKCICPPYKENS  
GHIYNKNIS  
QKDCDCLHVVEPMPVRGPDVEAYCLRCECKYEERSSVTIKVTII IYLSILGLLLLYMVYLT  
L  
VEPILKRRLFGHAQLIQSDDDIGDHQPFANAHDVLA  
RSRANVLNKVEYAQQRWKLQVQEQ  
RKSVFDRHVVL

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FIGURE 301

GCACCTGCGACCAACCGTGAGCAGTCAATGGCGTACTCCACAGTGCAGAGAGTCGCTCTGGCTT  
CTGGGCTTGTCCTGGCTCTGTCGCTGCTGCTGCCCAAGGCCTTCCTGTCCCGCGGGAAGCGG  
CAGGAGCCGCCGCCGACACCTGAAGGAAAATTGGGCCGATTTCCACCTATGATGCATCATCA  
CCAGGCACCCTCAGATGGCCAGACTCCTGGGGCTCGTTTTCCAGAGGTCTCACCTTGCCGAGG  
CATTTGCAAAGGCCAAAGGATCAGGTGGAGGTGCTGGAGGAGGAGGTAGTGGAAGAGGTCTG  
ATGGGGCAGATTATTCCAATCTACGGTTTTGGGATTTTTTTATATATACTGTACATTCTATT  
TAAGGTAAGTAGAATCATCCTAATCATATTACATCAATGAAAAATCTAATATGGCGATAAAAA  
TCATTGTCTACATTAAAACTTCTTATAGTTCATAAAATTATTTCAAATCCATCATCTCTTTA  
AATCCTGCCTCCTCTTCATGAGGTACTTAGGATAGCCATTATTTCAGTTTCACATAAGAATG  
TTTACTCAATGTTTAAAGTGTTTTGCCCCAAAATTCACAACATAACAAGGCAGAACTAGGACTT  
GAACATGGATCTTTTGGTTCTTAATCCAGTGAGTGATACAATTCAATGCACTCCCCTGCCA

FIGURE 302

MAYSTVQRVALASGLVLALSLLLPKAFLSRGKRQEPPPTPEGKLGRFPPMMHHHQAPSDGQT  
PGARFQRSHLAEAFKAKGSGGGAGGGGSGRGLMGQIIPYGFIFLYILYILFKVSRIILI  
ILHQ

FIGURE 303

CGGCTCGAGTGCAGCTGTGGGGAGATTTCACTGCATTGCCTCCCCTGGGTGCTCTTCATCTT  
GGATTTGAAAGTTGAGAGCAGCATGTTTTGCCCCTGAAACTCATCCTGCTGCCAGTGTTAC  
TGGATTATTCCTTGGGCCTGAATGACTTGAATGTTTTCCCCGCCTGAGCTAACAGTCCATGTG  
GGTGATTCAAGCTCTGATGGGATGTGTTTTCCAGAGCACAGAAGACAAATGTATATTCAAGAT  
AGACTGGACTCTGTACCAGGAGAGCACGCCAAGGACGAATATGTGCTATACTATTACTCCA  
ATCTCAGTGTGCCTATTGGGCGCTTCCAGAACCGCGTACACTTGATGGGGGACATCTTATGC  
AATGATGGCTCTCTCCTGCTCCAAGATGTGCAAGAGGCTGACCAGGGAACCTATATCTGTGA  
AATCCGCCTCAAAGGGGAGAGCCAGGTGTTCAAGAAGGCGGTGGTACTGCATGTGCTTCCAG  
AGGAGCCCCAAAGAGCTCATGGTCCATGTGGGTGGATTGATTGAGATGGGATGTGTTTTCCAG  
AGCACAGAAGTGAAACACGTGACCAAGGTAGAATGGATATTTTCAGGACGGCGCGCAAAGGA  
GGAGATTGTATTTTCGTTACTACCACAACTCAGGATGTCTGTGGAGTACTCCCAGAGCTGGG  
GCCACTTCCAGAATCGTGTGAACCTGGTGGGGGACATTTTCCGCAATGACGGTTCCATCATG  
CTTCAAGGAGTGAGGGAGTCAGATGGAGGAACTACACCTGCAGTATCCACCTAGGGAACCT  
GGTGTTCAGAAAACCATTTGTGCTGCATGTGAGCCCGGAAGAGCCTCGAACACTGGTGACCC  
CGGCAGCCCTGAGGCCTCTGGTCTTGGGTGGTAATCAGTTGGTGATCATTGTGGGAATTGTC  
TGTGCCACAATCCTGCTGCTCCCTGTTCTGATATTGATCGTGAAGAAGACCTGTGGAAATAA  
GAGTTCAGTGAATTCTACAGTCTTGGTGAAGAACACGAAGAAGACTAATCCAGAGATAAAAG  
AAAAACCCTGCCATTTTGAAAGATGTGAAGGGGAGAAACACATTTACTCCCCAATAATTGTA  
CGGGAGGTGATCGAGGAAGAAGAACCAAGTGAAAAATCAGAGGCCACCTACATGACCATGCA  
CCCAGTTTGGCCTTCTCTGAGGTGAGATCGGAACAACTCACTTGAAAAAAGTCAGGTGGGG  
GAATGCCAAAAACACAGCAAGCCTTTTGAGAAGAATGGAGAGTCCCTTCATCTCAGCAGCGG  
TGGAGACTCTCTCCTGTGTGTGCTTGGGCCACTCTACCAGTGATTTGAGACTCCCGCTCTC  
CCAGCTGTCTCCTGTCTCATTGTTTGGTCAATACACTGAAGATGGAGAATTTGGAGCCTGG  
CAGAGAGACTGGACAGCTCTGGAGGAACAGGCCTGCTGAGGGGAGGGGAGCATGGACTTGGC  
CTCTGGAGTGGGACACTGGCCCTGGGAACAGGCTGAGCTGAGTGGCCTCAAACCCCCGTT  
GGATCAGACCCTCCTGTGGGCAGGGTTCTTAGTGGATGAGTTACTGGGAAGAATCAGAGATA  
AAAACCAACCCAAATCAA

FIGURE 304

MFCPLKLILLPVLLDYSGLNDLNVSPPELTVHVGDSALMGCVFQSTEDKCIFKIDWTLSPG  
EHAKDEYVLYYYSNLSVPIGRFQNRVHLMGDILCNDGSLLLQDVQEADQGTYICEIRLKGES  
QVFKKAVVLHVLPEEPKELMVHVGGLIQMGCVFQSTEVKHVTKVEWIFSGRRAKEEIVFRYY  
HKLMSVEYSQSWGHFQNRVNLVGDI FRNDGSIMLQGVRES DGGNYTCSIHLGNLVFKKTIV  
LHVSPEEPRTLVT PAALRPLVLGGNQLV IIVGIVCATILLLPVLILIVKKT CGNKSSVNSTV  
LVKNTKKTNP EIKEKPCHFERCEGEKHIYSPI IIVREVI EEEEPSEKSEATYMTMHPVWPSLR  
SDRNNSLEKKSGGGMPKTQQAF

FIGURE 305

CTATGAAGAAGCTTCCTGGAAAACAATAAGCAAAGGAAAACAAATGTGTCCCATCTCACATG  
GTTCTACCCTACTAAAGACAGGAAGATCATAACTGACAGATACTGAAATTGTAAGAGTTGG  
AAACTACATTTTGCAAAGTCATTGAACTCTGAGCTCAGTTGCAGTACTCGGGAAGCCATGCA  
GGATGAAGATGGATACATCACCTTAAATATTAAAACTCGGAAACCAGCTCTCGTCTCCGTTG  
GCCCTGCATCCTCCTCCTGGTGGCGTGTGATGGCTTTGATTCTGCTGATCCTGTGCGTGGGG  
ATGGTTGTCTGGGCTGGTGGCTCTGGGGATTTGGTCTGTCTATGCAGCGCAATTACCTACAAGA  
TGAGAATGAAAATCGCACAGGAACCTCTGCAACAATTAGCAAAGCGCTTCTGTCAATATGTGG  
TAAAACAATCAGAACTAAAGGGCACTTTCAAAGGTCATAAATGCAGCCCCCTGTGACACAAAC  
TGGAGATATTATGGAGATAGCTGCTATGGGTTCTTCAGGCACAACTTAACATGGGAAGAGAG  
TAAGCAGTACTGCACTGACATGAATGCTACTCTCCTGAAGATTGACAACCGGAACATTGTGG  
AGTACATCAAAGCCAGGACTCATTTAATTCGTTGGGTCGGATTATCTCGCCAGAAGTCGAAT  
GAGGTCTGGAAGTGGGAGGATGGCTCGGTTATCTCAGAAAATATGTTTGAGTTTTTGGGAAGA  
TGGAAAAGGAAATATGAATTGTGCTTATTTTCATAATGGGAAAATGCACCCTACCTTCTGTG  
AGAACAAACATTATTTAATGTGTGAGAGGAAGGCTGGCATGACCAAGGTGGACCAACTACCT  
TAATGCAAAGAGGTGGACAGGATAACACAGATAAGGGCTTTATTGTACAATAAAAGATATGT  
ATGAATGCATCAGTAGCTGAAAAAAAAAAAAA

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FIGURE 306

MQDEDGYITLNIKTRKPALVSVGPASSSWVRMALILLILCVGMVVGLVALGIWSVMQRNYL  
QDENENRTGTLQQLAKRFCQYVVKQSELKGTFFKGHKCSPCDTNWRYYGDSCYGFRRHNLWE  
ESKQYCTDMNATLLKIDNRNIVEYIKARTHLIRWVGLSRQKSNEVWKWEDGSVISENMFEDL  
EDGKGNMNCAYFHNGKMHPTFCENKHYLMCERKAGMTKVDQLP

(30) 60/088,742	10 Jun/juin 1998 (10.06.1998)	US	(30) 60/090,254	22 Jun/juin 1998 (22.06.1998)	US	(30) 60/091,478	2 Jul/jul 1998 (02.07.1998)	US
(30) 60/088,810	10 Jun/juin 1998 (10.06.1998)	US	(30) 60/090,355	23 Jun/juin 1998 (23.06.1998)	US	(30) 60/091,626	2 Jul/jul 1998 (02.07.1998)	US
(30) 60/088,811	10 Jun/juin 1998 (10.06.1998)	US	(30) 60/090,349	23 Jun/juin 1998 (23.06.1998)	US	(30) 60/091,628	2 Jul/jul 1998 (02.07.1998)	US
(30) 60/088,824	10 Jun/juin 1998 (10.06.1998)	US	(30) 60/090,429	24 Jun/juin 1998 (24.06.1998)	US	(30) 60/091,633	2 Jul/jul 1998 (02.07.1998)	US
(30) 60/088,825	10 Jun/juin 1998 (10.06.1998)	US	(30) 60/090,431	24 Jun/juin 1998 (24.06.1998)	US	(30) 60/091,646	2 Jul/jul 1998 (02.07.1998)	US
(30) 60/088,826	10 Jun/juin 1998 (10.06.1998)	US	(30) 60/090,435	24 Jun/juin 1998 (24.06.1998)	US	(30) 60/091,673	2 Jul/jul 1998 (02.07.1998)	US
(30) 60/088,858	11 Jun/juin 1998 (11.06.1998)	US	(30) 60/090,444	24 Jun/juin 1998 (24.06.1998)	US	(30) 60/091,978	7 Jul/jul 1998 (07.07.1998)	US
(30) 60/088,861	11 Jun/juin 1998 (11.06.1998)	US	(30) 60/090,445	24 Jun/juin 1998 (24.06.1998)	US	(30) 60/091,982	7 Jul/jul 1998 (07.07.1998)	US
(30) 60/088,863	11 Jun/juin 1998 (11.06.1998)	US	(30) 60/090,461	24 Jun/juin 1998 (24.06.1998)	US	(30) 60/092,182	9 Jul/jul 1998 (09.07.1998)	US
(30) 60/088,876	11 Jun/juin 1998 (11.06.1998)	US	(30) 60/090,472	24 Jun/juin 1998 (24.06.1998)	US	(30) 60/092,472	10 Jul/jul 1998 (10.07.1998)	US
(30) 60/089,090	12 Jun/juin 1998 (12.06.1998)	US	(30) 60/090,535	24 Jun/juin 1998 (24.06.1998)	US	(30) 60/093,339	20 Jul/jul 1998 (20.07.1998)	US
(30) 60/089,105	12 Jun/juin 1998 (12.06.1998)	US	(30) 60/090,538	24 Jun/juin 1998 (24.06.1998)	US	(30) 60/094,651	30 Jul/jul 1998 (30.07.1998)	US
(30) 60/089,440	16 Jun/juin 1998 (16.06.1998)	US	(30) 60/090,540	24 Jun/juin 1998 (24.06.1998)	US	(30) 60/095,282	4 Aug/aout 1998 (04.08.1998)	US
(30) 60/089,512	16 Jun/juin 1998 (16.06.1998)	US	(30) 60/090,557	24 Jun/juin 1998 (24.06.1998)	US	(30) 60/095,285	4 Aug/aout 1998 (04.08.1998)	US
(30) 60/089,514	16 Jun/juin 1998 (16.06.1998)	US	(30) 60/090,676	25 Jun/juin 1998 (25.06.1998)	US	(30) 60/095,301	4 Aug/aout 1998 (04.08.1998)	US
(30) 60/089,532	17 Jun/juin 1998 (17.06.1998)	US	(30) 60/090,678	25 Jun/juin 1998 (25.06.1998)	US	(30) 60/095,302	4 Aug/aout 1998 (04.08.1998)	US
(30) 60/089,538	17 Jun/juin 1998 (17.06.1998)	US	(30) 60/090,688	25 Jun/juin 1998 (25.06.1998)	US	(30) 60/095,318	4 Aug/aout 1998 (04.08.1998)	US
(30) 60/089,598	17 Jun/juin 1998 (17.06.1998)	US	(30) 60/090,690	25 Jun/juin 1998 (25.06.1998)	US	(30) 60/095,321	4 Aug/aout 1998 (04.08.1998)	US
(30) 60/089,599	17 Jun/juin 1998 (17.06.1998)	US	(30) 60/090,691	25 Jun/juin 1998 (25.06.1998)	US	(30) 60/095,325	4 Aug/aout 1998 (04.08.1998)	US
(30) 60/089,600	17 Jun/juin 1998 (17.06.1998)	US	(30) 60/090,694	25 Jun/juin 1998 (25.06.1998)	US	(30) 60/095,916	10 Aug/aout 1998 (10.08.1998)	US
(30) 60/089,653	17 Jun/juin 1998 (17.06.1998)	US	(30) 60/090,695	25 Jun/juin 1998 (25.06.1998)	US	(30) 60/095,929	10 Aug/aout 1998 (10.08.1998)	US
(30) 60/089,801	18 Jun/juin 1998 (18.06.1998)	US	(30) 60/090,696	25 Jun/juin 1998 (25.06.1998)	US	(30) 60/096,012	10 Aug/aout 1998 (10.08.1998)	US
(30) 60/089,907	18 Jun/juin 1998 (18.06.1998)	US	(30) 60/090,862	26 Jun/juin 1998 (26.06.1998)	US	(30) 60/096,143	11 Aug/aout 1998 (11.08.1998)	US
(30) 60/089,908	18 Jun/juin 1998 (18.06.1998)	US	(30) 60/090,863	26 Jun/juin 1998 (26.06.1998)	US	(30) 60/096,146	11 Aug/aout 1998 (11.08.1998)	US
(30) 60/089,947	19 Jun/juin 1998 (19.06.1998)	US	(30) 60/091,358	1 Jul/jul 1998 (01.07.1998)	US	(30) 60/096,329	12 Aug/aout 1998 (12.08.1998)	US
(30) 60/089,948	19 Jun/juin 1998 (19.06.1998)	US	(30) 60/091,360	1 Jul/jul 1998 (01.07.1998)	US	(30) 60/096,757	17 Aug/aout 1998 (17.08.1998)	US
(30) 60/089,952	19 Jun/juin 1998 (19.06.1998)	US	(30) 60/091,544	1 Jul/jul 1998 (01.07.1998)	US	(30) 60/096,766	17 Aug/aout 1998 (17.08.1998)	US
(30) 60/090,246	22 Jun/juin 1998 (22.06.1998)	US	(30) 60/091,486	2 Jul/jul 1998 (02.07.1998)	US	(30) 60/096,768	17 Aug/aout 1998 (17.08.1998)	US
(30) 60/090,252	22 Jun/juin 1998 (22.06.1998)	US	(30) 60/091,519	2 Jul/jul 1998 (02.07.1998)	US	(30) 60/096,773	17 Aug/aout 1998 (17.08.1998)	US
						(30) 60/096,791	17 Aug/aout 1998 (17.08.1998)	US



(30) 60/096,867 17 Aug/oct 1998 US  
 (17.08.1998)  
 (30) 60/096,891 17 Aug/oct 1998 US  
 (17.08.1998)  
 (30) 60/096,894 17 Aug/oct 1998 US  
 (17.08.1998)  
 (30) 60/096,895 17 Aug/oct 1998 US  
 (17.08.1998)  
 (30) 60/096,897 17 Aug/oct 1998 US  
 (17.08.1998)  
 (30) 60/096,949 18 Aug/oct 1998 US  
 (18.08.1998)  
 (30) 60/096,950 18 Aug/oct 1998 US  
 (18.08.1998)  
 (30) 60/096,959 18 Aug/oct 1998 US  
 (18.08.1998)  
 (30) 60/096,960 18 Aug/oct 1998 US  
 (18.08.1998)  
 (30) 60/097,022 18 Aug/oct 1998 US  
 (18.08.1998)  
 (30) 60/097,141 19 Aug/oct 1998 US  
 (19.08.1998)  
 (30) 60/097,218 20 Aug/oct 1998 US  
 (20.08.1998)  
 (30) 60/097,661 24 Aug/oct 1998 US  
 (24.08.1998)  
 (30) 60/097,951 26 Aug/oct 1998 US  
 (26.08.1998)  
 (30) 60/097,952 26 Aug/oct 1998 US  
 (26.08.1998)  
 (30) 60/097,954 26 Aug/oct 1998 US  
 (26.08.1998)  
 (30) 60/097,955 26 Aug/oct 1998 US  
 (26.08.1998)  
 (30) 60/097,971 26 Aug/oct 1998 US  
 (26.08.1998)  
 (30) 60/097,974 26 Aug/oct 1998 US  
 (26.08.1998)  
 (30) 60/097,978 26 Aug/oct 1998 US  
 (26.08.1998)  
 (30) 60/097,979 26 Aug/oct 1998 US  
 (26.08.1998)  
 (30) 60/097,986 26 Aug/oct 1998 US  
 (26.08.1998)  
 (30) 60/098,014 26 Aug/oct 1998 US  
 (26.08.1998)  
 (30) 60/098,525 31 Aug/oct 1998 US  
 (31.08.1998)  
 (30) 60/100,634 16 Sept/sep 1998 US  
 (16.09.1998)  
 (30) 60/115,565 12 Jan/jan 1999 US  
 (12.01.1999)

